

American Journal of Obstetrics and Gynecology

VOL. 43

FEBRUARY, 1942

No. 2

American Association of Obstetricians, Gynecologists and
Abdominal Surgeons

Fifty-Fourth Annual Meeting, September 11 to 13, 1941

A COMPARISON OF THYROID EXTRACT AND IODINE THERAPY IN THE PREVENTION OF TOXEMIA OF PREGNANCY*

EMMETT D. COLVIN, M.D., R. A. BARTHOLOMEW, M.D., AND
WILLIAM H. GRIMES, M.D., ATLANTA, GA.

(From the Department of Obstetrics, Emory University, School of Medicine)

DURING the past few years we have endeavored to lessen, or to prevent, if possible, the occurrence of true toxemia by the administration of thyroid extract and, more recently, by the use of iodine during pregnancy.

The rationale, supporting the use of these agents, is based on certain facts developed from previous investigations, dealing mainly with the placenta. The most important fact is that certain types of placental infarcts are so consistently associated with toxemia of pregnancy that one may predict the type of infarct which will be found in the placenta of a patient who has developed toxemia, and, vice versa, one may assert the presence or absence of toxemia during pregnancy from examination of an "unknown" formalin-fixed placenta.¹ Of great significance is the fact that the extent or mass of the infarction bears a definite relation to the severity of the toxemia.

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

Another significant fact is that placental tissue contains a greater amount of arginine than any other tissue.² This amino acid, when oxidized in the course of autolysis of infarcted placental tissue, may theoretically liberate guanidine.³ Repeated injections of autolysate of placental tissue produce convulsions and death in animals.⁴ Autolysate from other tissues produces toxic effects but not convulsions.⁵

While guanidine has been demonstrated in increased amounts in pre-eclampsia and eclampsia,⁶⁻⁸ the test is not only difficult, but it is recognized that poisonous amino acids do not remain in the blood but quickly become fixed in the tissues.⁹ Repeated injections of guanidine in animals produce arteriolar spasm, hypertension, albuminuria, hypoglycemia, liver and kidney damage, increase in uric acid, convulsions, and death. These manifestations are strikingly similar to those seen in pre-eclampsia and eclampsia.

Since infarction implies obstruction in the circulation to the involved area, it is of interest to note that visible evidence of thrombosis has not only been found, affecting some of the large vessels on the fetal surface of the placenta, but a predisposing cause of thrombosis has been found in the presence of a layer or collection of fat-laden cells beneath the endothelium of many of the placental vessels.¹⁻⁴ This predisposes to roughening or breaking down of the endothelium from the trauma of fetal movements. The appearance of placental vessels affected in this manner is very similar to that seen in coronary thrombosis, and also that seen in the aorta and coronaries of cholesterol-fed rabbits.¹⁰

The physiologic hypercholesterolemia of pregnancy has long been known and recognized; also the fact that when the basal metabolism is low, the blood cholesterol is increased and vice versa. Since basal metabolism has been found to be definitely lower in the Southeast¹¹ and mortality associated with pregnancy definitely higher in this region,¹² it is possible that a greater degree of hypercholesterolemia may be a predisposing factor.

Furthermore, Hunt, Patterson and Nicodemus,¹³ acting upon this suggestion found that thyroidectomized, cholesterol-fed pregnant rabbits developed a typical eclamptic syndrome near term, whereas control pregnant rabbits, cholesterol-fed but not thyroidectomized, did not show this effect. The placentas from the rabbits having convulsions showed typical acute infarcts. The placental vessels showed piling up of fat cells beneath the endothelium to such a degree that the lumen was blocked. It appeared, therefore, that preservation of the thyroid prevented excessive cholesterol-vascular change in the placental vessels, thereby preventing infarction, convulsions, and death.

Finally, Turner¹⁴ has demonstrated that typical cholesterol vascular change is produced in the arteries of experimental animals when fed cholesterol. He further proves that the blood cholesterol content of the animals increased if cholesterol is administered in the diet. He found that the administration of thyroid extract concurrently with cholesterol prevented hypercholesterolemia and atheromatous changes

in the aortas of 89 per cent of the animals studied. Likewise, he demonstrated that potassium iodide administered along with cholesterol was effective in preventing hypercholesterolemia and vascular changes in 91 per cent of the animals. The mechanism of this protection was obscure. In order to determine the influence of the thyroid gland, cholesterol and potassium iodide were fed concurrently to thyroidectomized animals. Thyroidectomy in itself did not cause hypercholesterolemia or the development of atheromatous changes in the aorta. Feeding cholesterol produced hypercholesterolemia and vascular changes regardless of the presence or absence of the thyroid gland. In thyroidectomized animals, the protective influence of potassium iodide in preventing cholesterol vascular changes in cholesterol-fed rabbits was lost.

Based on the above facts and reasoning as to the possible benefits of thyroid extract or iodine in limiting or preventing cholesterol-vascular change in the placental vessels and thus lessening the incidence of infarction and toxemia, a series of private patients was given thyroid extract (Parke, Davis & Co.) throughout pregnancy. The dose, which varied from 1.5 to 3 gr. daily was determined early in pregnancy and subsequently controlled by repeated basal metabolism tests and observation of the patient's reactions. Owing to the increased susceptibility of hypothyroid cases to toxemia, only those with minus metabolism were treated. For obvious reasons, it was not possible to make repeated blood cholesterol determinations throughout pregnancy.

At the end of the thyroid study, another series of cases was studied as to the effect of iodine treatment. The preparation originally used in dose of one capsule daily (1.08 gr.) was discontinued after a short time on account of objectionable bulk and unpleasant eructation. Lipiodine (Ciba), one tablet daily, containing a comparable dose (1.8 gr. iodine), was substituted and found to be more palatable and free of undesirable effects. Only five cases in the iodine treated series developed visible and palpable enlargement of the thyroid, which subsided on discontinuing the drug. Iodine treatment was routinely stopped at the end of the eighth month on the presumption that inhibition of cholesterol-vascular change need not be carried beyond this stage.

Since hypertension was one of the more important criteria in determining the development of toxemia, a diastolic pressure of 80 mm. of mercury, based on the last distinct sound, was taken as the upper limit of normal. The systolic pressure being more variable and subject to more influences, was not considered sufficiently reliable. Since the diastolic pressure is 60 to 70 mm. of mercury in more than 80 per cent of normal patients throughout pregnancy,¹⁵ it is necessary to regard a rise above 80 mm. as an indication of impending toxemia, necessitating more careful and frequent observation. It is probably un-

safe to ignore a rising diastolic pressure until it has reached the generally accepted level of 90 mm. as the upper limit of normal. The associated development of retinal arteriolar spasms, increasing albuminuria, uric acid, edema, headache, and other symptoms is relied upon as further evidence.

It must not be presumed that a moderate rise in blood pressure and albumin late in pregnancy necessarily means true toxemia of pregnancy. In both the thyroid and iodine series of cases, the differentiation of hypertension due to early vascular disease and that due to true toxemia was made by retinal examination early and late in pregnancy and also by examination of the formalin-fixed placenta.

In a recent study,¹⁵ we were able to show that latent or mild vascular disease, as shown by a slight disturbance of the normal arteriovenous ratio of 2 to 3, to one between 1 to 2 and 2 to 3 or occasionally 1 to 2, and slight increase in light reflex, are present in 16 to 20 per cent of patients who show no hypertension early in pregnancy. Two-thirds of these patients develop mild to moderate hypertension and albuminuria in the last four to six weeks of pregnancy, apparently due to renal pathology and not due to true toxemia of pregnancy. The accompanying symptoms of edema and headache are very mild and there is seldom need for interrupting the pregnancy. The blood pressure is more variable and more responsive to rest in bed than in the case of true toxemia. The placentas from these cases show no toxic types of infarcts unless there has been evidence of a superimposed toxemia. The greater the disturbance in A-V ratio (1 to 3 or 1 to 4, etc.) the earlier the onset of hypertension in pregnancy. Of the patients showing disturbances in A-V ratio, nearly all were mild in type, between 1 to 2 and 2 to 3, a few 1 to 2 and rarely 1 to 3.

Since Chesley and Chesley¹⁶ have shown that the result of the cold pressor test early in pregnancy is inconstant and that the response is essentially the same in pretoxic and prenatal groups, we believe that retinal examination will prove to be more reliable.

In this study the cases were divided into early vascular disease and normal types according to the retinal findings early in pregnancy as seen in Table I.

TABLE I. INCIDENCE OF MILD VASCULAR DISEASE IN 760 CASES

GROUP	CASES	PER CENT
Mild vascular disease	171	22.5
Normal	589	77.5

Mild vascular disease group includes patients found to have increased light reflex over retinal arteries and A-V ratio between 1 to 2 and 2 to 3, occasionally 1 to 2 and rarely 1 to 3

A diagnosis of toxemia, whether superimposed on vascular disease or arising in normal cases late in pregnancy, was based on the development

of localized spasms of the retinal arterioles, increase in blood uric acid, and a greater degree of albuminuria, headache, edema, and hypertension than in vascular disease cases. Retinal arteriolar spasms are absent in hypertension due to mild vascular disease, and the symptoms and findings are milder, seldom necessitating interruption of pregnancy. Finally examination of the formalin-fixed placenta indicated true toxemia, if the toxic types of infarcts were found or vascular disease if they were absent.

Since the susceptibility to toxemia and the need for treatment were judged by the results of the basal metabolism tests early in pregnancy, the cases were divided into the following groups.

TABLE II. BASAL METABOLIC RATE IN 698 CASES

RATE	CASES	PER CENT
-10 or lower	263	37.6
-10 to 0	264	35.2
0 to +10	147	21.1
+10 or higher	42	6.1

This table does not include 62 additional cases in which basal metabolic rate was not determined

Two-thirds of the cases showed basal metabolic rates of zero or less. This finding further emphasizes that basal metabolic rates are lower in the southern than the northern states. Since a low metabolic rate predisposes to toxemia, this may have bearing on the higher incidence of toxemia in the Southeast.

Since iodine proved to be so much more potent than thyroid extract in preventing true toxemia of pregnancy, as will be shown in a subsequent table, the trend of the basal metabolic rate in the vascular disease and the normal cases, is compared in Table III, to determine whether the difference could be explained on this basis.

TABLE III. COMPARISON OF BASAL METABOLIC RATE IN 539 NORMAL CASES AND 159 MILD VASCULAR DISEASE CASES

B.M.R.	NORMAL		VASCULAR DISEASE	
	CASES	PER CENT	CASES	PER CENT
-10 or lower	208	38.6	55	34.6
-10 to 0	188	34.8	58	36.4
0 to +10	114	21.2	33	20.8
+10 or higher	29	5.4	13	8.2

The results show there is no significant difference in the basal metabolic rates in the early vascular disease and the normal groups, and the difference in the effect of iodine treatment must be explained on some other basis.

The results of the administration of thyroid extract to both normal and early vascular disease cases are shown in Table IV.

TABLE IV. EFFECT OF THYROID EXTRACT ON INCIDENCE OF TOXEMIA

GROUP	CASES	NON-TREATED	TOXEMIA	TREATED	TOXEMIA
Mild vasc. disease	83	48	7 (14.6%)	35	5 (14.3%)
Normal	240	155	34 (21.9%)	85	23 (27.0%)

Contrary to the results obtained by Hughes¹⁷ who showed a reduction of 50 per cent in the incidence of toxemia, the above analysis fails to show any benefit by treatment with thyroid extract.

The results of the administration of iodine to both normal and early vascular disease cases are shown in Table V.

TABLE V. EFFECT OF IODINE ON INCIDENCE OF TOXEMIA

GROUP	CASES	NON-TREATED	TOXEMIA	TREATED	TOXEMIA
Mild vasc. disease	88	49	3 (6.1%)	39	2 (5.1%)
Normal	349	161	41 (25.4%)	188	12 (6.4%)

For some unaccountable reason, the administration of iodine to cases of vascular disease during pregnancy fails to lower the already low incidence of toxemia in these cases, but when administered to normal cases, the frequency of toxemia is reduced almost 75 per cent. Whether this remarkable benefit is brought about through the effects anticipated in the rationale of the treatment or in some other manner, endocrine or otherwise, we are not prepared to say although the former view is favored.

Objection may be raised that the adoption of 80 as the upper limit of normal diastolic pressure permits the inclusion of too many cases of mild toxemia, which would otherwise be excluded by adoption of the usually accepted figure of 90. As we have already stated, practical experience necessitates the adoption of the lower figure inasmuch as one cannot safely ignore the early manifestations of toxemia which occur in the range of 80 to 90 diastolic pressure.

However, for the sake of comparison with the generally accepted standard of 90 as the upper limit of diastolic blood pressure in pregnancy, the cases have been divided into mild (diastolic from 80 to 90); moderately severe (90 to 100); severe (100 or above), also eclampsia and abruptio. Other symptoms and findings of toxemia were also considered in classifying the cases into these groups. Table VI shows the effect of iodine treatment in toxemias of various degrees of severity.

TABLE VI. INCIDENCE AND DEGREE OF TOXEMIA IN IODINE AND NONTREATED NORMAL CASES

GROUP	CASES	DEGREE OF TOXEMIA				
		MILD	MODERATE	SEVERE	ECLAMPSIA	ABRUPTIO
Nontreated	161	28 (17.4%)	7 (4.3%)	3 (1.3%)	1 (0.6%)	2 (1.3%)
Iodine treated	188	6 (3.2%)	3 (1.6%)	2 (1.1%)	0	1 (0.5%)

Although improvement is most marked in the mild cases, the more severe grades of toxemia are noticeably benefited. It is conceivable that prevention of cholesterol-vascular change and preservation of adequate circulation in the placental vessels lowers the incidence of mild toxemia; this in turn must be reflected in a lower incidence of the more severe forms of toxemia.

In Table VII, a comparison of the effect of thyroid extract and iodine in preventing toxemia is shown in the cases of early vascular disease.

TABLE VII. COMPARISON OF RESULTS OF THYROID EXTRACT AND IODINE THERAPY IN PREVENTING TOXEMIA IN MILD VASCULAR DISEASE CASES

GROUP	CASES	TOXEMIA	
		CASES	PER CENT
Control cases	97	10	10.3
Thyroid treated	35	5	14.3
Iodine treated	39	2	5.1

The results indicate that the incidence of toxemia superimposed on early vascular disease is reduced 50 per cent by the use of iodine, whereas thyroid extract apparently exerts no benefit.

In Table VIII a comparison of the effects of thyroid extract and iodine in preventing toxemia is shown in the normal cases.

TABLE VIII. COMPARISON OF RESULTS OF THYROID EXTRACT AND IODINE THERAPY IN PREVENTING TOXEMIA IN NORMAL CASES

GROUP	CASES	TOXEMIA	
		CASES	PER CENT
Control cases	316	75	23.1
Thyroid treated	85	23	27.0
Iodine treated	188	12	6.4

The results indicate that in normal cases as well as in early vascular disease cases, thyroid extract does not confer any protection against the development of toxemia. The administration of iodine, however, exerts a marked protection and reduces the later development of toxemia more than 75 per cent.

In Table IX, the incidence of severe toxemia, comprising the moderately severe, severe, eclamptic and abruptio cases taken as a group, is compared in the nontreated and iodine treated cases.

TABLE IX. INCIDENCE OF MODERATE AND SEVERE TOXEMIA INCLUDING ECLAMPSIA AND ABRUPTIO PLACENTAE IN 349 CASES

GROUP	CASES	TOXEMIA
Nontreated	161	13 (8.1%)
Iodine treated	188	6 (3.2%)

This table excludes mild types of toxemia.

The results indicate that the severe forms of toxemia are reduced nearly two-thirds or 60 per cent, by the administration of iodine during pregnancy.

DISCUSSION

If one attempts to evaluate the benefit of any therapeutic agent administered during pregnancy to lower the incidence of toxemia, he must recognize that certain cases developing evidences of mild or moderate toxemia late in pregnancy, are not cases of true toxemia but are cases of mild or latent vascular disease. Retinal examination early in pregnancy and again after development of toxic symptoms and findings, is of the greatest aid in differentiating vascular disease from true toxemia. Examination of the formalin-fixed placenta furnished the final proof in judging whether the toxic manifestations were due to true toxemia or to vascular disease.

It would have been desirable had the study covered a larger series of cases in both the thyroid and iodine treated groups, but the benefit of iodine in reducing the incidence of toxemia is so striking that we feel that a larger series of cases would not materially alter the results.

Furthermore, considering the fact that we have taken the last distinct sound rather than the beginning of the last phase as the diastolic pressure, also the fact that treatment has been limited to the group most susceptible to toxemia, and that a certain number of cases of toxemia occur in cases showing normal or slightly elevated basal metabolism, it is reasonable to believe that the possible beneficial results of iodine treatment have been under- rather than overstated.

We would emphasize again the usefulness of the ophthalmoscope to the obstetrician; also the satisfaction to be obtained from familiarity with the types of placental infarcts in the final classification of the case.

Inasmuch as toxemia may occur in any pregnancy, regardless of the basal metabolic rate and since lipoiodine (Ciba), in a dose of one tablet daily, is pleasant to take and is well tolerated, it would seem unnecessary to subject pregnant patients to basal metabolic tests, but routinely administer one tablet of lipoiodine daily from the end of the third month, when nausea and vomiting have usually ceased, on to full term. This dose is well tolerated, even though the patient may also be using iodized salt. The simplicity and apparent efficacy of this treatment recommends it as a valuable routine, both for private patients and for prenatal clinics supervised by departments of public health.

CONCLUSIONS

1. True toxemia and vascular disease should be differentiated in evaluating the efficacy of any prophylactic treatment of true toxemia of pregnancy.
2. The ophthalmoscope is a most valuable aid in differentiating true toxemia of pregnancy and vascular disease during pregnancy.

3. Examination of the formalin-fixed placenta for toxic types of infarcts is essential in the final classification of the disorder.

4. By the usually accepted standard, the basal metabolic rate in pregnancy is definitely lower in the Southeast than in other sections of the United States.

5. Low basal metabolism is a predisposing factor in the development of true toxemia of pregnancy and may be a contributing factor to the higher incidence of toxemia in the Southeast.

6. Hypercholesterolemia, induced both by pregnancy and a lower basal metabolic rate, predisposes to cholesterol-vascular change in the placental vessels.

7. Cholesterol-vascular change in the placental vessels is the probable antecedent to thrombosis, infarction, and true toxemia of pregnancy.

8. In pregnant animals, experimentation has shown the striking protective value of iodine and thyroid extract in the prevention of cholesterol-vascular change.

9. In women, administration of iodine markedly lowers the frequency of all degrees of toxemia during pregnancy; thyroid extract apparently confers no protection.

10. Lipoiodine (Ciba) is a pleasant, well-tolerated form of iodine; it does not require an initial or subsequent determination of the basal metabolic rate and, given routinely in a dose of one tablet (1.8 gr. iodine) daily from the end of the third month to full term, gives promise of effecting a great reduction in the frequency of true toxemia of pregnancy.

REFERENCES

1. Bartholomew, R. A., and Colvin, E. D.: *AM. J. OBST. & GYNEC.* **36**: 909, 1938.
2. Harding, V. C., and Fort, C. H.: *J. Biol. Chem.* **35**: 29, 1918.
3. Bartholomew, R. A., and Parker, F.: *AM. J. OBST. & GYNEC.* **27**: 72, 1934.
4. Bartholomew, R. A., and Kracke, R. R.: *AM. J. OBST. & GYNEC.* **24**: 797, 1932.
5. Oden, C. L. A.: *J. Mich. State M. Soc.* **24**: 110, 1925.
6. Minot, A. S., and Cutler, J. T.: *Proc. Soc. Exper. Biol. & Med.* **26**: 607, 1929.
7. Andes, et al.: *J. Lab. & Clin. Med.* **23**: 9, 1937.
8. Malmejac, J.: *Rev. franç. de gynéc. et d'obst.* **25**: 435, 1930.
9. Wells, *Chemical Pathology*, ed. 5, p. 66.
10. Leary, T.: *Arch. Path.* **17**: 453, 1934.
11. Talbot, F. B., Wilson, E. B., and Worcester, Jane: *Am. J. Dis. Child.* **53**: 273, 1937.
12. United States Bureau of the Census, Department of Labor.
13. Patterson, W. B., Hunt, H. F., and Nicodemus, R. E.: *Am. J. Clin. Path.* **8**: 120, 1938.
14. Turner, Kenneth B.: *J. Exper. Med.* **58**: 115, 1933.
15. Bartholomew, R. A., and Colvin, E. D.: *AM. J. OBST. & GYNEC.* **42**: 646, 1941.
16. Chesley, L. C., and Chesley, Eliz. R.: *Surg., Gynec. & Obst.* **69**: 436, 1939.
17. Hughes, E. C.: *AM. J. OBST. & GYNEC.* **40**: 48, 1940.

1259 CLIFTON ROAD, N. E.

DISCUSSION

DR. ROBERT A. ROSS, DURHAM, N. C.—The authors, among other things, stress information obtained by the arteriovenous ratio. Unfortunately their data regarding this are not yet published. The light reflex, to be of value, must be done by the

same person, at the same time of day and under constant conditions, as other disturbing factors give spasm of the retinal vessels.

For a long while the amino acids have been indicted as the cause of eclampsia, but different workers pick different acids. Johnston and Johnston think it is tyramine, others pick histamine and various other products. The authors think guanidine may be causative, but correctly state that the quantitations are a bit uncertain and that this amino acid does not remain in the blood very long.

The hypercholesterolemia of pregnancy is generally known, and there is a further slight rise in toxemia. This rise, according to our observations, is in the cholesterol esters. This unusual ratio between the free and combined cholesterol may have some significance. Our series of toxic patients show a hypoproteinemia, and it is our feeling that this lack may call for a compensatory increase in the fats and sterols in order to maintain osmotic pressure.

Iodine is one of the oldest therapeutic agents, but we have been unable to prove that it influences cholesterol metabolism in the human being.

In order to understand correctly the theme of this paper, it would seem that one should accept the placental infarct theory of eclampsia, then reason that iodine is given to alter the blood cholesterol so that there would be no vascular depositions, then no thrombosis, no infarction with its increase in arginine and thus no guanidine. The authors are careful thinkers and observers but the thesis is complicated.

DR. HERMAN W. JOHNSON, HOUSTON, TEXAS.—We like to give Dr. Young, an Honorary Member of this Society, credit for being the first one to associate placental infarction with eclampsia. I believe, however, that he had a predecessor. Young carried his theory down to a split protein which today we are not justified in doing as the chemistry of protein has made long strides since 1914.

In our earlier papers we thought like Young that the infarcted area was the source of the toxic amine. This idea was abandoned several years ago. If the toxic substance were in the infarcted area, the fetus should be more affected than the mother. Our theory now places the source of the toxic amine in the degenerated chorionic epithelium, and this being adjacent to the intervillous spaces accounts for the mother being more often affected than the child.

We believe that eclamptic toxemia is associated with the upright position, because the human female is the only animal that has eclampsia. This upright position, together with other conditions of pressure—namely first pregnancies, advanced pregnancy, oversized babies, twins, and polyhydramnios—results in stasis in the intervillous spaces. This stasis causes in various areas degeneration of the chorionic epithelium. For a number of years we assumed this degeneration of the chorionic epithelium took place but had no proof of it. It has now been shown that in the severe pre-eclamptic the syncytium is degenerated in 80 per cent of the villi and that in normal pregnancy only 20 per cent showed degeneration.

Cell autolysis then gives rise in these areas of degeneration to loosely held amino acids. Bacterial enzymes, if present in the blood, may convert the amino acids, especially tyrosine, into tyramine. If the condition of uniform pressure exists, namely living fetus and unruptured membranes, tyramine is absorbed by the maternal circulation. If absorbed, it causes in the nonsensitive patient hypertension alone. In the sensitive patient it produces hypertension plus angiospasm often leading to convulsions. Repeated skin tests show convulsive patients extremely sensitive to weak dilutions of tyramine.

DR. E. F. SHUTE, LONDON, CANADA.—I agree with Dr. Colvin on the importance of hypothyroidism in the etiology of the toxemias and on the importance of recognizing and treating toxemias *very* early, at the first albuminuria, at the first edema,

or at the first hypertension. If the treatment is not begun then one can scarcely expect to prevent their development, although their severity may be mitigated.

Patients who have a lack of thyroid do not excrete estrogen well and therefore, presumably, the estrogens pile up, producing conditions which I think are responsible for most of the late toxemias. The best antiestrogens appear to be progesterone and vitamin E. If one uses vitamin E in these late toxemias associated with high estrogen values, the dose should be large. A certain small percentage of these late toxemias are true pre-eclampsics, are associated with low estrogen values and improve on estradiol or stilbestrol. In these latter, we have used as much as 50,000 international units of estradiol two or three times a week, or 5 mg. of stilbestrol per day. Our results are of interest and will be summarized in the near future.

DR. COLVIN (closing).—In answer to a question, we encountered only 5 cases reacting unfavorably to lipoiodine. All developed tenderness and enlargement over the area of the thyroid gland which immediately disappeared when the iodine was discontinued.

In regard to the origin of placental infarcts, we remain convinced of the specificity of infarcts associated with true toxemia of pregnancy. The infarcts are on the fetal side of the circulation and due to interference of the fetal circulation in placental vessels. It does not seem logical to believe that a poisonous substance circulating in the maternal blood stream could produce localized infarcts without involving the entire exposed surface of the placenta.

In dealing with the problem of hypertension and albuminuria late in pregnancy, one must bear in mind that all such cases are not true toxemia. The ophthalmoscopic investigation of the retinal arteries early and late in pregnancy along with a carefully conducted study of the formalin-fixed placenta for acute infarcts will aid in the differential diagnosis and final classification. We have found that approximately one-fifth of our cases reveal evidence of vascular disease early in pregnancy. The increased light reflex over the sclerosed retinal arteries along with a disturbance in the arteriovenous ratio are usually the only characteristics by which such cases are to be recognized. More than 60 per cent of these patients develop hypertension and albuminuria four to six weeks before term. The management of such cases is different from that of true toxemia.

Although lipoiodine is not effective in preventing superimposed toxemia in vascular disease cases, the fact that it is capable, in doses of $4\frac{1}{2}$ gr., of reducing the incidence of true toxemia approximately 75 per cent in normal cases should warrant its more extensive use.

GRANULOSA AND THECA CELL TUMORS OF THE OVARY*

WITH A REPORT OF THIRTY CASES

D. NELSON HENDERSON, M.D., TORONTO, ONTARIO

(From the Departments of Obstetrics and Gynecology and Pathology of the University of Toronto)

THIS paper is a report of a clinical and pathologic study of 21 cases of granulosa cell tumors and 9 cases of theca cell tumors of the ovary. These tumors have all been encountered during the past twelve years.† The case histories are complete and with three exceptions include a postoperative follow-up record of from one to twelve years. The close relationship between the granulosa and theca cell type of tumor is recognized, but they will be discussed separately because of the controversy regarding the pathologic status of the latter.

The twenty-one granulosa cell neoplasms presented considerable variation in gross and microscopic appearance. The smallest tumor was microscopic in size while the largest weighed 24 pounds. The moderate-sized tumors, as a rule, revealed areas of interstitial hemorrhage, cystic degeneration, and necrosis (Fig. 1, A). The solid portions were whitish in color and of brainlike consistency. Marked friability was a constant feature of those tumors which were predominantly of the follicular type. One tumor presented gross evidence of luteinization. This tumor measured 6 cm. in diameter and the cut surface was a brilliant yellow color, presenting the appearance of a huge corpus luteum of pregnancy (Fig. 1, B). The tumors, with one exception, could be divided into the three generally accepted microscopic types: the follicular, the cylindroid or trabecular, and the sarcomatoid (Fig. 2, A, B, C). More than one type was usually present in a single tumor and frequently all three were found. One tumor was of an adenomatous type. Traut and Butterworth¹ and Varangot² have described similar tumors but they are rare (Fig. 2, D).

The diagnosis of the follicular and cylindroid type of granulosa cell tumor offered little difficulty. The pattern of growth was distinctive and the granulosa cells closely resembled the normal granulosa cell of the Graafian follicle. Tumors of the sarcomatoid type were frequently more difficult to recognize as granulosa cell neoplasms. The granulosa cells in both appearance and manner of growth had lost their distinc-

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

†The clinical and pathologic features of these cases are summarized in Tables V and VI.

tive epithelial character and resembled connective tissue cells. If sufficient sections were examined, however, areas of transition of these connective tissuelike cells to typical or nearly typical granulosa cells

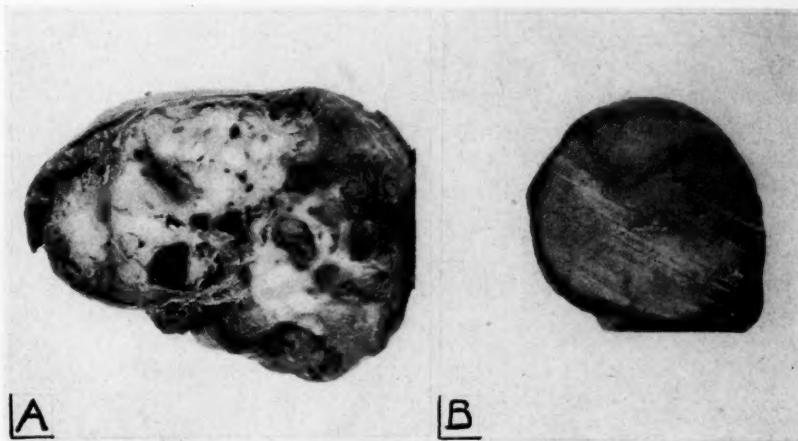


Fig. 1.—(A) Granulosa cell tumor showing interstitial hemorrhage, cystic degeneration, and necrosis. (B) Completely luteinized granulosa cell tumor. The cut surface was a brilliant yellow color. This tumor occurred before puberty.

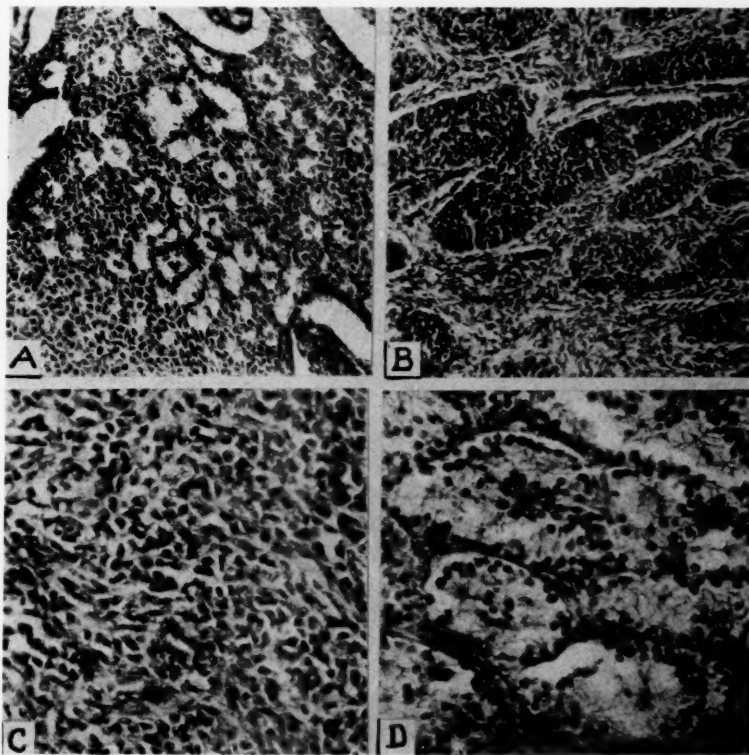


Fig. 2.—Four microscopic types of granulosa cell tumor: (A) follicular, (B) cylindroid, (C) sarcomatoid, and (D) adenomatous.

could be found, as well as a change in manner of growth from sarcoma-like to follicular or cylindroid.

As no hormone assays were made, evidence of biologic activity of the tumor was obtained from the clinical history or the microscopic examination of the endometrium. The common clinical evidence of hormone activity was uterine bleeding alternating with irregular periods of amenorrhea. Amenorrhea of three to four months' duration was common while periods as long as two years were occasionally observed. When such long periods of amenorrhea occurred during the age period of the menopause it was often difficult to determine whether the amenorrhea was due to a physiologic menopause or to the tumor. Endometrial hyperplasia of the Schroeder or "Swiss-cheese" type was the common pathologic evidence of excessive estrogen secretion. During the post-menopausal years, myometrial hypertrophy frequently accompanied the

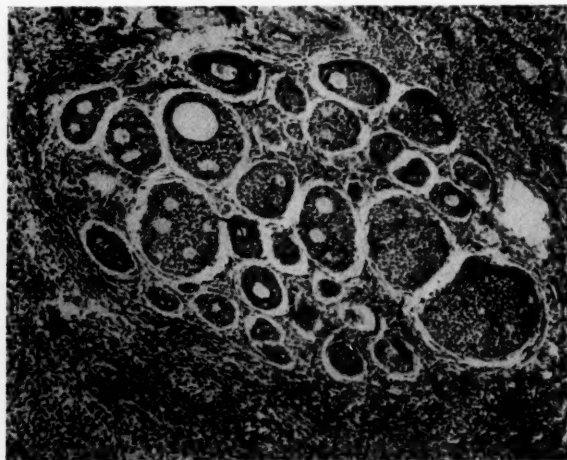


Fig. 3.—Microscopic granulosa cell tumor. This tumor was found in an ovary removed along with a pregnant uterus at the time of therapeutic abortion.

endometrial hyperplasia while, in the one case occurring before puberty, secondary sex characteristics were precociously developed. Evidence of biologic activity of the tumor was present in 15 of the 21 cases. In 10 cases the evidence was endometrial hyperplasia and in 5 it was a clinical history of irregular uterine bleeding. In 4 of these 5 cases, the endometrium was not available for study, while in the fifth case the endometrium was in the early proliferative phase.

Of the 6 tumors which were classified as failing to produce evidence of biologic activity, 2 were associated with carcinoma of the endometrium and the uterine bleeding which occurred in these cases was attributed to this lesion. Of the remaining 4 tumors, 2 were of the follicular type and 2 of the sarcomatoid. The smallest tumor and the largest in the series were in this group of neoplasms which failed to

produce evidence of estrogen secretion. The smallest tumor was microscopic in size and was accidentally found in an ovary removed along with a pregnant uterus at the time of therapeutic abortion (Fig. 3).

In the group of 21 granulosa cell tumors, there were 5 cases of uterine fibroids as well as 2 cases of carcinoma of the endometrium. As those findings were duplicated with the theca cell neoplasms, their possible significance will be discussed later. Dockerty and MacCarty³ have reported 2 cases of carcinoma and 8 cases of fibroids in a group of 30 granulosa cell tumors.

The age incidence of the tumors (Table I) corresponds fairly closely with other reported series. Excluding the one case which occurred before puberty, 9 occurred before and 11 after the menopause. As previously mentioned, however, it is often difficult to determine whether amenorrhea occurring at the age period of the menopause is due to a physiologic climacteric or the result of the estrogen secreted by the tumor.

TABLE I. GRANULOSA CELL GROUP

Under 10 years	1 case
Over 20 years	1 case
30 years	4 cases
40 years	5 cases
50 years	6 cases
60 years	2 cases
70 years	2 cases

The postoperative follow-up record (Table II) reveals one clinically malignant tumor, a remarkably low incidence of malignancy when compared with the 15.4 per cent reported by Traut and Marchetti,⁴ 28.1 per cent, by Novak,⁵ and an estimated 25 per cent by Varangot.²

TABLE II. GRANULOSA CELL GROUP, FOLLOW-UP RECORD

NO. OF CASES	PRESENT STATE	DURATION OF FOLLOW-UP
5	Alive and well	7 to 12 years
6	Alive and well	4 to 6 years
7	Alive and well	1 to 3 years
1	Died postoperative	21 days
1	Died from recurrence	3 months
1	Unknown	

The effect of postoperative high voltage x-ray treatment was difficult to evaluate. Six patients received radiotherapy. One of these patients died three months after operation with ascites and evidence of abdominal carcinomatosis. This tumor was judged histologically malignant. Of the remaining five tumors, only two were considered histologically malignant and both patients are alive and well, one for five years and one for eight years. As no definite histologic basis for the diagnosis of malignancy has been established for these tumors, the last

two cases do not warrant any conclusions. The failure of the high voltage treatment to arrest the progress of the growth in the one case is similar to the experience of Traut⁴ who concluded that "in the malignant group of tumors x-ray is not effective in retarding or stopping the progress of the growth." Nevertheless, until more is known about the malignant potentialities of the granulosa cell tumor and the effect of irradiation on a large number of cases has been observed, it would seem wise to advise such treatment in all cases in which the tumor occurs at the time of, or after, the menopause.

Considerable variation in the rate of growth of these neoplasms was evident. One patient was observed for three and one-half years without any increase in size of the neoplasm, while the largest tumor in the series occurred in a patient, whose only complaint was a rapidly enlarging abdomen for one year. Another case demonstrated marked rapidity of growth following the intrauterine application of radium for metrorrhagia. The radium was inserted under anesthesia and no ovarian enlargement was noted at that time. Three months later a malignant sarcomatoid type of granulosa cell tumor, 16 cm. in diameter, was removed. The abdomen was filled with blood-stained fluid and the tumor showed extensive interstitial hemorrhage and necrosis. Traut⁴ mentions two tumors which were apparently unaffected by previously applied intrauterine radium.

The clinical and pathologic status of the theca cell tumor cannot be as exactly defined as that of the granulosa cell neoplasm.

Since Loeffler and Priesel¹² first described a fibroma-like tumor of the ovary, having estrogenic effects, as a fibroma thecacellulare xanthomatoides ovarii, doubt has arisen of the actual existence of a theca cell tumor and of its biologic activity. Thomson and Sabler,⁶ in a critical review of the cases reported by Geist¹³ as well as the above authors, state that these authors "have not succeeded in proving their case as to the existence of a special group of tumors with specific naked eye and histologic appearance and typical symptomatology." Novak⁵ questions the advisability of too sharp a division between the granulosa and theca cell tumors and considers them "a species of granulosa cell neoplasm." Traut,⁴ in analyzing 54 cases of what he termed "so-called granulosa and theca cell tumors," found only 4 pure theca cell neoplasms and none gave evidence of hormone secretion.

It is not the purpose of this paper to present a critical review of this discussion but rather to outline the clinical and pathologic features of our cases judged to belong to this rather uncertain group of neoplasms.

Briefly, our diagnosis of a theca cell tumor has been made on: (1) A firm fibromalike tumor with a cut surface presenting streaks or islands of yellowish colored tissue which stand out rather prominently. In one case, the whole tumor was distinctly yellow (Fig. 4). (2) A microscopic picture of interlacing bundles of connective tissue cells with

rather broad spindle-shaped nuclei. Scattered throughout this connective tissue network are islands of epithelioid cells, either with vacuolated cytoplasm or acidophilic cytoplasm and clearly defined polyhedral cell

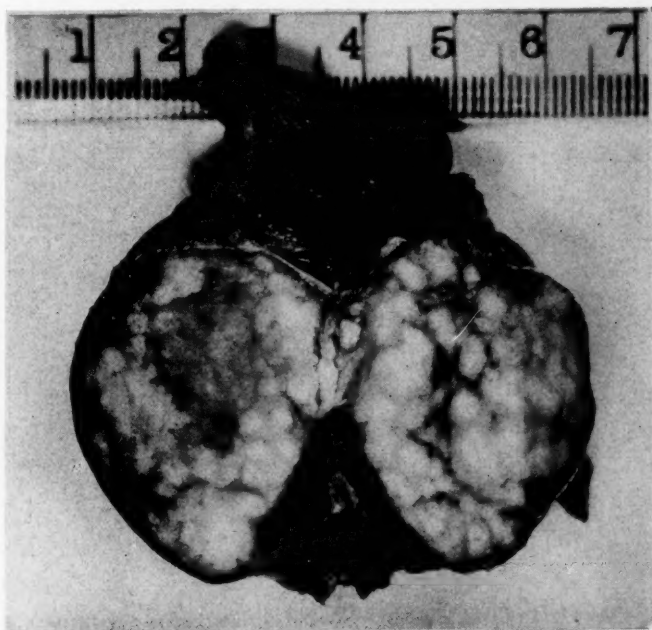


Fig. 4.—Theca cell tumor.

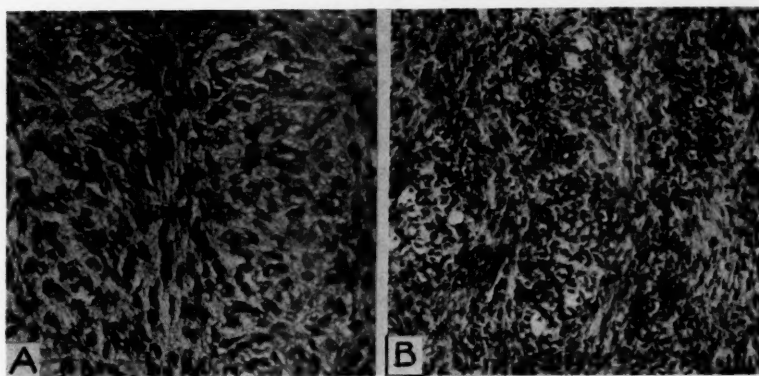


Fig. 5.—Microscopic features of theca cell tumor. (A) Interlacing bundles of connective tissue cells with rather broad spindle-shaped nuclei; (B) islands of vacuolated epithelial-like cells.

boundaries giving a luteinlike appearance to the cells. Extensive areas of hyalinization are usual. (Figs. 5 and 6, A, B, C.) (3) The presence of varying amounts of intracellular lipoid (Fig. 6, D).

Only one of the 9 tumors occurred before the menopause. In this case menstruation was normal and the endometrium was in the premenstrual phase. The remaining eight tumors were all associated with

uterine bleeding. In 5 the bleeding was associated with endometrial hyperplasia and in 3 with carcinoma of the endometrium. One of the cases of hyperplasia was atypical and four years after the original diagnosis of hyperplasia had been made a second curettage revealed adenocarcinoma. The uterus was the site of fibroids in 5 of the 9 cases. Wolfe and Neigus⁷ have recently reported one case of carcinoma of the endometrium and 4 cases of fibroids in a group of 8 theca cell tumors.

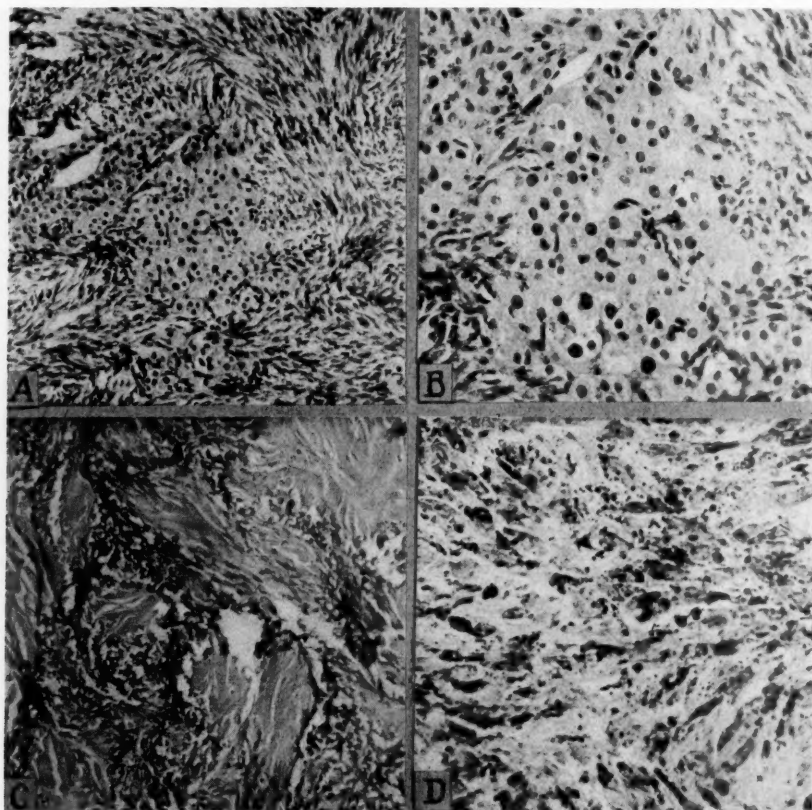


Fig. 6.—Microscopic features of theca cell tumor. (A) and (B) Low and high power of luteinized cells; (C) areas of hyaline degeneration; (D) intra- and extracellular lipid as demonstrated by sudan III.

The age incidence of the theca cell tumors was later than that of the granulosa group (Table III). With one exception all occurred after fifty years of age.

TABLE III. THECA CELL TUMORS, AGE INCIDENCE

YEARS	NO. OF CASES
30-39	1 case
40-49	0 cases
50-59	4 cases
60-69	3 cases
70-79	1 case

The postoperative follow-up record (Table IV) reveals that none of these tumors has proved to be malignant. Three patients received postoperative high voltage x-ray treatment.

All the theca cell and the majority of the granulosa cell tumors were stained by Laidlaw's silver stain to demonstrate reticulum. As pointed

TABLE IV. THECA CELL TUMORS, FOLLOW-UP

NO. OF CASES	PRESENT STATE	DURATION OF FOLLOW-UP
1	Alive and well	7 years
1	Alive and well	6 years
1	Alive and well	4 years
1	Alive and well	3 years
3	Alive and well	1-2 years
1	Alive and well	6 months then lost
1	Unknown	

out by both Brosig⁸ and Traut^{4, 9} granulosa cells are reticulum free and theca cells are individually surrounded by it. In the theca cell neoplasms, chains and islands of reticulum-free cells were found in every tumor (Fig. 7, A, B). These reticulum-free cells were not necessarily those which showed vacuolization of their cytoplasm or lutein transformation. The luteinized cells when found in large clumps were almost invariably reticulum free (Fig. 8, A), whereas cells identical in appearance when few in number were occasionally individually surrounded by reticulum, but more frequently were clustered together in groups of three or four by a reticular network (Fig. 8, B). We were unable to form a definite opinion in regard to the theca or granulosa nature of these luteinized cells. In the granulosa cell tumors, particularly those of the trabecular and cylindroid type, the septa between the cords of granulosa cells contained cells enmeshed in reticulum which closely resembled theca cells (Fig. 9).

Varying degrees of luteinization occurred in both groups of tumors. In the granulosa cell group luteinization of the accompanying theca-like cells was frequently noted when such change was absent in the granulosa cells. Two granulosa cell tumors were completely luteinized (Fig. 10). The first, which occurred before puberty, was a brilliant yellow color and on microscopic examination was of the adenomatous type. Unfortunately, no endometrium was available for study in this case but the clinical history left no doubt in regard to the biologic activity of the tumor. The second granulosa cell tumor, which was completely luteinized, failed to produce evidence of biologic activity. Microscopic luteinization was not synonymous with the presence of intracellular lipid. In some of the theca cell tumors, areas showing the heaviest deposition of fat failed to present the microscopic characteristics of luteinization. It was noted also that the degree of luteinization of the tumor bore no relationship to the type of uterine bleeding or to periods of amenorrhea.

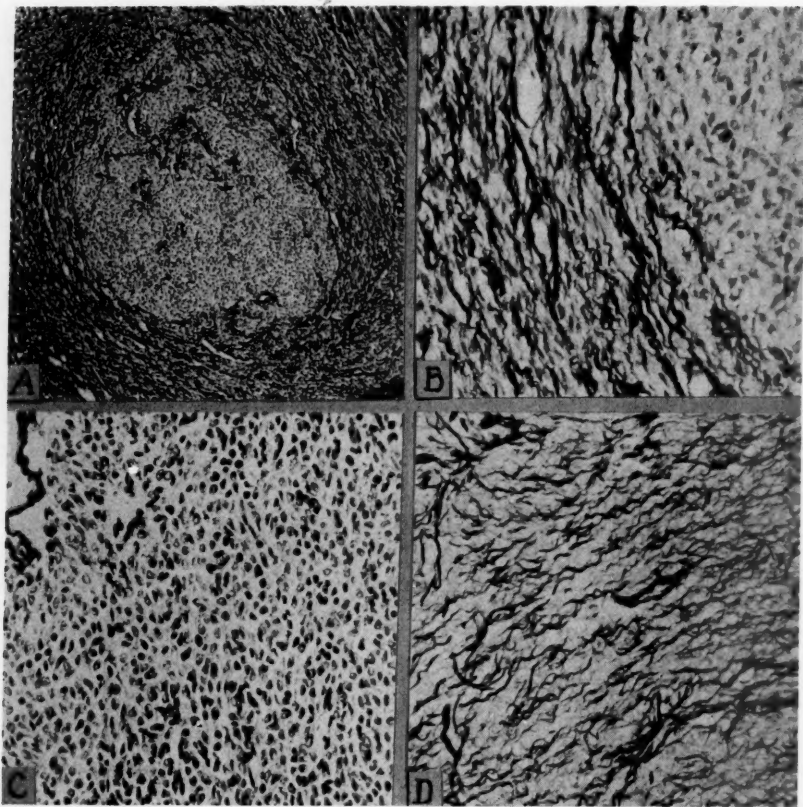


Fig. 7.—Reticulum stain. (A) An island of reticulum-free cells in a theca cell tumor, (B) high power at margin of the island; (C) sarcomatoid type of granulosa cell tumor—no reticulum; (D) reticulum of theca cell tumor.

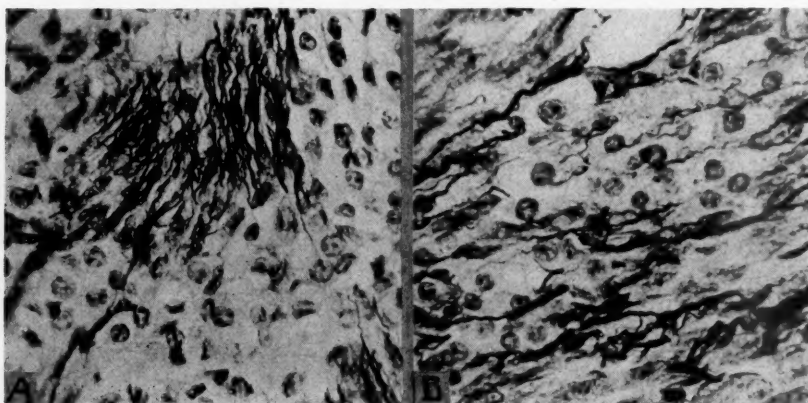


Fig. 8.—(A) Luteinized reticulum-free cells in theca cell tumor; (B) cells similar in appearance but individually surrounded by reticulum as well as arranged in cords and small groups by a reticular network.

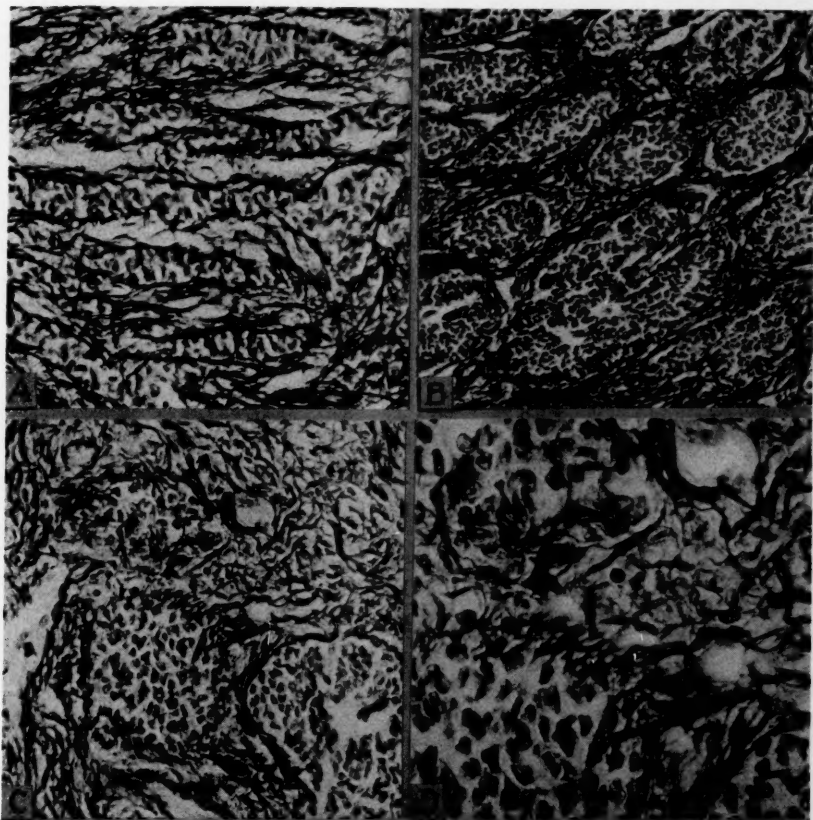


Fig. 9.—Reticulum stain, granulosa cell tumors. (A) Trabecular type; (B) cylindroid type; (C) two islands of reticulum-free granulosa cells are seen at the bottom of the microphotograph. In the septum above these granulosa cells are theca-like cells individually surrounded by reticulum; (D) high power magnification showing both types of cells.

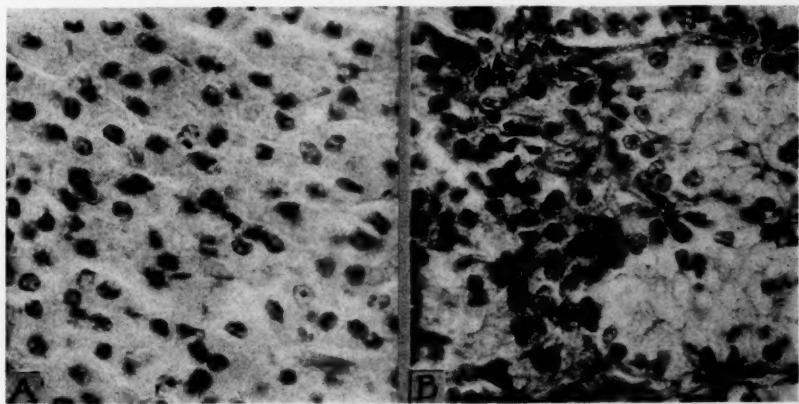


Fig. 10.—Photomicrographs of the two extensively luteinized granulosa cell tumors. (A) Luteinlike cells without vacuolization; (B) extensive vacuolization of cells in adenomatous type of tumor. Tumor B gave clinical evidence of hormone secretion while A did not.

TABLE V. GRANULOSA CELL GROUP

CLINICAL SUMMARY				PATHOLOGIC SUMMARY				
AGE	PARA	ENDOCRINE DISTURBANCE	OPERATION	FOLLOW-UP	SIZE	TYPE	ENDOMETRIUM	UTERUS
20	2	None	Oophorectomy	Alive and well 6 years	15 cm.	Luteoma	No	No
39	6	Irregular bleeding two years' duration	Hysterectomy Bil. T. & O.*	None	5 cm.	Follicular	Hyperplasia	Hypertrophied
39	3	Irregular bleeding with long periods of amenorrhea, 4 years' duration	Oophorectomy	Alive and well 7 years	20 cm.	Follicular and cylindroid	No	Hypertrophied
36	0	Irregular bleeding with amenorrhea, 3 years' duration	Hysterectomy Bil. T. & O.	Alive and well 6 years	8 cm.	Follicular	Hyperplasia	Fibroids
7	0	Vaginal bleeding and precocious development of secondary sex characteristics	Oophorectomy	Alive and well 6 years	4 cm.	Luteoma, adenomatous type	No	No
48	Unknown	Amenorrhea 2 years with hot flushes	Oophorectomy	Alive and well 2 years	24 lb.	Sarcomatoid and follicular	No	No
44	2	Irregular bleeding 2 years' duration	D & C. Bil. T. & O.	Alive and well 14 months	22 cm.	Cylindroid and follicular	Hyperplasia	No
49	4	Prolonged menstruation, flow lasting 14 days, 1 yr. duration	Hysterectomy Bil. T. & O.	Alive and well 14 months	2 cm.	Follicular and cylindroid	Postmenstrual	Fibroids
46	1	Irregular bleeding	Bil. T. & O.	Alive and well 9 years	10 cm.	Cylindroid	No	No
37	2	None, patient pregnant at operation	Hysterectomy Bil. T. & O.	Alive and well 10 months	Microscopic	Follicular	Pregnant	Pregnant

*Bil. T. & O., Bilateral salpingo-oophorectomy.

72	1	Irregular bleeding 3 months' duration	Hysterectomy Bil. T. & O.	Died postoperative	26 cm.	Sarcomatoid and cylindroid	Hyperplasia	Atrophied
57	3	Amenorrhea 3 years' duration. Vaginal bleeding 1 month	Hysterectomy Bil. T. & O.	Alive and well 1 year	20 cm.	Sarcomatoid	Hyperplasia	Hypertrophied
55	3	Irregular bleeding 2 years' duration	Hysterectomy Bil. T. & O.	Alive and well 12 years	1 cm.	Follicular and cylindroid	Hyperplasia	Hypertrophied
59	2	Endometrial hyperplasia treated by hysterectomy 1924. Ovarian tumor 1934	Oophorectomy	Alive and well 8 years	24 cm.	Sarcomatoid and cylindroid	Hyperplasia 1924	Hypertrophied 1924
60	Multiple	Irregular bleeding 2 years' duration	Bil. T. & O.	Alive and well 3 years	13 cm.	Sarcomatoid and follicular	Hyperplasia	Hypertrophied
70	1	Irregular bleeding 6 months' duration	Hysterectomy Bil. T. & O.	Alive and well 1½ years	4½ cm.	Sarcomatoid and cylindroid	Adenocarcinoma	Hypertrophied
59	0	Irregular bleeding 18 months' duration	Hysterectomy Bil. T. & O.	Alive and well 5½ years	2 cm.	Follicular	Adenocarcinoma	Hypertrophied and fibroids
66	6	Vaginal bleeding 1 week	Hysterectomy Bil. T. & O.	Alive and well 4 years	3 cm.	Follicular and cylindroid	Hyperplasia and polypus	Fibroids
51	Unknown	Vaginal bleeding 3 months' duration	Oophorectomy	Died 3 months	16 cm.	Sarcomatoid	No	No
51	2	Irregular bleeding 2 years' duration	Repair Hysterectomy Bil. T. & O.	Alive and well 7 years	3 cm.	Follicular	Hyperplasia	Fibroids
42	7	Irregular bleeding 6 months' duration	Hysterectomy Bil. T. & O.	Alive and well 6 years	2½ cm.	Sarcomatoid and follicular	Hyperplasia	Hypertrophied

TABLE VI. THECA CELL GROUP

AGE	PARA	CLINICAL SUMMARY			FOLLOW-UP	PATHOLOGIC SUMMARY		
		ENDOCRINE DISTURBANCE	OPERATION			SIZE	ENDOMETRIUM	UTERUS
37	2	Menstruation normal	Hysterectomy Bil. T. & O.	Alive and well 7 years		10 cm.	Premenstrual	Fibroids
72	0	Irregular bleeding one year duration	Hysterectomy Bil. T. & O.	Alive and well 1 year		8 cm.	Adenocarcinoma	
60	1	Vaginal bleeding 4 years. Curetting 1934, atypical hyperplasia Curetting 1938, carcinoma	Hysterectomy Bil. T. & O.	Alive and well 3 years		2 cm.	Adenocarcinoma	Fibroids
56	Unknown	Bleeding, 1 year duration	Hysterectomy Left oophorectomy	Alive and well 6 months (then lost)		2 cm.	Atypical hyperplasia	Fibroids
55	5	No bleeding	Vaginal Hysterectomy Right oophorectomy	Alive and well 1 year		4½ cm.	Hyperplasia	Fibroids
63	2	Vaginal bleeding, 5 months' duration	Hysterectomy Bil. T. & O.	Alive and well 18 months		4 cm.	Hyperplasia	Hypertrophied
66	5	Vaginal bleeding, 9 months' duration	Hysterectomy Bil. T. & O.	Alive and well 6 years		8 cm.	Hyperplasia	Adenomyosis
57	2	Vaginal bleeding, 4 months' duration	Hysterectomy Bil. T. & O.	Alive and well 4 years		1 cm.	Adenocarcinoma	Adenocarcinoma
50	0	Vaginal bleeding, one year duration	Hysterectomy Bil. T. & O.	Unknown		2 cm.	Hyperplasia	Adenomyosis and fibroids

The occurrence of 5 cases of carcinoma of the endometrium in this series of 30 tumors suggests a relationship between prolonged estrogen stimulation of the endometrium, endometrial hyperplasia and carcinoma. Only one carcinoma was a localized tumor. It was of a papillary type situated in the fundus of the uterus and had deeply invaded the myometrium. The remaining 4 cases had the following common pathologic features. The endometrium was diffusely involved and the myometrium only superficially invaded. The glandular arrangement, while markedly irregular and of a bizarre pattern, was well maintained. The glandular epithelium was of a secretory type and the supporting stroma was very scant in amount. The possibility that these cases only represented extreme degrees of benign hyperplasia was considered but after careful review by the author as well as Prof. W. L. Robinson, it was decided that no diagnosis other than carcinoma was justified. However, none of these patients has died from cancer or suffered from recurrence. Is it possible that the changes in the endometrium which fulfilled the requirements for the diagnosis of carcinoma in this site were completely dependent upon the estrogen secreted by the ovarian tumor and did not represent true neoplasia?

The significance of 10 cases of uterine fibroids is equally difficult to evaluate. Excessive or prolonged secretion of estrogen has been suggested as a cause for fibroids, but there is little convincing evidence to support such a theory. On the contrary there is considerable evidence that ovarian function is normal in regard to ovulation and endometrial response in the majority of cases of uterine fibroids.^{10, 11} In 2 of these 10 cases, the endometrium was not of the hyperplasia pattern but was of the normal cyclic pattern for the known phase of the menstrual cycle. The possibility of some relationship between the estrogen-secreting ovarian neoplasm and the uterine tumors should be considered, but a definite conclusion of direct relationship is unwarranted.

SUMMARY

Thirty ovarian tumors belonging to the granulosa and theca cell group of neoplasms are reported. They correspond in age incidence, clinical manifestations, and in gross and microscopic appearance with other reported cases. They differ in one major respect, that of malignancy. Only one tumor has proved to be malignant despite a follow-up record of four years or longer in 14 cases. By means of Laidlaw's silver stain granulosa-like cells were identified in all theca cell tumors and thecalike cells in a number of granulosa cell neoplasms. While our results are similar to those reported by Traut and Marchetti, we are not yet completely satisfied in regard to the recognition of these two types of cells by this method. Tumors of the theca cell group, however, had a later age incidence and presented sufficiently well-marked pathologic differences to warrant their continued recognition as a particular

type of estrogen-secreting tumor. Two of the granulosa cell tumors were completely luteinized and one of these was of the unusual adenomatous type. The occurrence of 5 cases of carcinoma of the endometrium and 10 cases of uterine fibroids suggests a direct relationship between the ovarian neoplasm and the uterine tumors but does not warrant a definite conclusion in this regard.

Twenty-six of these tumors were encountered in the pathologic laboratory of the Toronto General Hospital, 2 in the Toronto Western Hospital, and 2 in the Ontario Provincial Health Laboratory. I am indebted to Dr. George Shanks and Dr. S. F. Penny for the surgical specimens from the 4 outside cases. I am also indebted to Drs. H. B. Coleman, J. L. Robinson, R. W. Wesley, R. R. Graham, N. Shenstone, and R. B. Hare for the clinical histories and follow-up records of their cases, as well as to my associates of the gynecologic staff of the Toronto General Hospital for similar records of their private cases. One case has been previously reported by Dr. Hare in *Canad. M. Assn. J.* 36: 620, 1937. This case which occurred before puberty was included in the present series because of the follow-up record now available and the complete luteinization of the tumor which was not emphasized in the original report.

REFERENCES

1. Traut, H. F., and Butterworth, J. S.: *AM. J. OBST. & GYNEC.* 34: 987, 1937.
2. Varangot, J.: *J. de Chir.* 51: 651, 1938.
3. Dockerty, M. B., and MacCarty, W. C.: *AM. J. OBST. & GYNEC.* 37: 426, 1939.
4. Traut, H. F., and Marchetti, A. A.: *Surg. Gynec. & Obst.* 70: 632, 1940.
5. Novak, E., and Brawner, J.: *AM. J. OBST. & GYNEC.* 28: 637, 1934.
6. Thomson, J. G., and Sabler, F.: *J. Obst. & Gynaec. Brit. Emp.* 45: 769, 1938.
7. Wolfe, S. A., and Neigus, I.: *AM. J. OBST. & GYNEC.* 42: 218, 1941.
8. Brosig, W.: Quoted by Karsner, H. T.: *Trans. Coll. Phys., Philadelphia*, Ser. 7, No. 4, 1940.
9. Traut, H. F., Kuder, A., and Cadden, J. F.: *AM. J. OBST. & GYNEC.* 38: 798, 1939.
10. Brewer, J. I., and Jones, H. O.: *AM. J. OBST. & GYNEC.* 41: 733, 1941.
11. Henderson, D. N.: *AM. J. OBST. & GYNEC.* 41: 694, 1941.
12. Loeffler, E., and Priesel, A.: *Beitr. z. path. Anat. u. z. allg. Path.* 90: 199, 1932.
13. Geist, S. H.: *AM. J. OBST. & GYNEC.* 30: 481, 1935.

DISCUSSION

DR. EMIL NOVAK, BALTIMORE, MD.—Dr. Henderson has reported findings which correspond to those of other authors, with the one exception of malignancy rate. He reports only 1 case of recurrence, while the figures of others would indicate a recurrence rate of from 28 to 35 per cent. Certainly our own experience has not been nearly as favorable as Dr. Henderson's. In our first follow-up, a fraction over 28 per cent of recurrences were noted. We now have over 100 instances of this tumor type in our laboratory, although many of these were sent in from outside sources. It is obvious, however, that granulosa cell carcinoma is a fairly common neoplasm.

All are agreed that the degree of malignancy is very much less than that of ovarian cancer in general, and statistics on recovery rates from the latter are misleading unless cognizance is taken of this fact. The striking biologic phenomena produced by some granulosa cell tumors, particularly those in prepubertal and postmenopausal patients, may lead some to forget that the majority of these tumors occur during reproductive life, when the endocrine effects produced by such tumors are inconspicuous or lacking. When such tumors occur in children, before the ovaries assume their estrogenic function, the production of estrogen by the tumor brings about the phenomena of precocious puberty. When they arise long after the menopause, the uterus undergoes hypertrophy and menstruation-like bleeding is produced, although breast changes are absent, presumably because of the unresponsiveness of the senile breast to estrogen stimulation. During reproductive

life, however, the ovaries normally produce abundant estrogen and the sex characters are fully developed, so that the production of estrogen by the tumor is a purely quantitative factor, producing sometimes menstrual excess, sometimes amenorrhea of the so-called polyhormonal type, while often menstruation is quite normal.

I have been interested in Dr. Henderson's discussion of the occasional association of uterine adenocarcinoma with granulosa cell tumors. I note that his patients who showed this association were all postmenopausal, which was of special interest to me because, as some of you know, I have urged the view that postmenopausal estrogenic stimulation of the endometrium, as seen in cases of postmenopausal hyperplasia, may be a predisposing factor to the development of adenocarcinoma.

With reference to the histogenesis of these tumors, we are coming more and more to feel that their ultimate source is the ovarian mesenchyme, which is the progenitor of both the granulosa and theca. If such a feminizing mesenchymoma develops along epithelial lines, it becomes a granulosa cell tumor or one of its luteinized derivatives. If it assumes the connective tissue form, it develops into the thecoma, which likewise may undergo luteinization. However, I have never seen a thecoma in which granulosal elements were not also demonstrable, while the same admixture is also seen in many granulosa cell growths. For this reason, the granulosa cell tumor and the thecoma should not be so sharply separated as they have been by some authors.

There is one final point which I should like to stress as regards the production of precocious puberty by granulosa cell tumors. This rather spectacular phenomenon, and the equally spectacular results accomplished by removal of the tumor, have led some to assume the presence of such a growth whenever a case of female sex precocity presents itself. Nothing could be further from the truth, for a considerably larger number of cases are due to other causes, and most often no tumor of any endocrine organ is demonstrable. In cases of granulosa tumor etiology the precocious menstruation is not associated with ovulation. In certain cases of the extraovarian group, however, both menstruation and ovulation occur. Children of this type can therefore conceive at abnormally early ages, and this is obviously the explanation of such cases as the recent one, so widely publicized, of pregnancy in a 5-year-old Chilean girl.

DR. JAMES E. DAVIS, ANN ARBOR, MICH.—A phase of this study which is sometimes quite troublesome concerns the hyperplasias of the granulosa cells and theca cells. When correlation of these changes with the physiologic conditions is made, the question arises as to just how far the patient will carry these tissues before they reach the tumor stage.

Another interesting phase concerns the adequacy of criteria that one has before him at the time of each individual study. If a group of these cases are studied several years apart, differing criteria may be set up at each study. This is especially true with microscopic data, and differing conclusions will be reached. Diagnostic criteria are not yet very substantially established.

Another difficult factor in this study is that time is not available to study completely all of the tumor. One part of the tumor will often give an entirely different picture from that of another part. Hence it cannot be said that data are absolutely correct or comparable unless study is made of the entire tumor.

The point of theca cell tumors coming in the higher age group is interesting. Connective tissue will of course, increase as age increases, and I question whether in this particular study this does not account for the impression which sets apart the age groups. Some of the microscopic sections shown on the screen may well have been theca cell instead of granulosa cell tumors.

DR. HENDERSON (closing).—Dr. Novak talked of luteinization, which I did not have time to mention. Two of the tumors were completely luteinized, one occurring before puberty, the second later but without an associated disturbance of menstruation. In neither of these two tumors did we have endometrium available for study to say whether there was any secretory change.

I was interested in the fact that Dr. Davis felt on looking at the slides that all these tumors might well be considered as granulosa cell neoplasms. The relationship between the two types is so intimate that I would be quite willing to acquiesce in that suggestion. There were, however, differences which were more or less constant for the theca cell tumors and I grouped them together merely to draw your attention to these tumors again in order to establish their identity as a separate type of estrogen-secreting neoplasm.

MALIGNANCY OF THE OVARIES*

JAMES ROBERT GOODALL, B.A., M.D., C.M., D.Sc., F.R.C.O.G.,
F.I.C.S. (HON.), MONTREAL, QUE.

IN DEALING with so complex a subject, in which there are so many unknown elements, it would seem best to divide the subject matter into its main headings, and discuss each one separately.

They naturally fall into the following subdivisions:

1. Malignancy, its meaning and properties.
2. The ovary, as the source and generator, its properties and potentialities.

MALIGNANCY

The more one studies the vagaries of tissues, and the more one becomes experienced in the interpretation of their vital phenomena, the less is one inclined to define malignancy, and still less inclined to draw a definite line between tumors with malignant properties and those with benign attributes. In the minds of most pathologists there is a no man's land between malignancy and benignity, into which we have to throw a large number of ovarian tumors of questionable parentage and still more questionable adolescence and senescence.

The ovary has types of growths which are common to other organs. But it possesses also a potentiality for types of growth that are essentially and exclusively ovarian. Does not this last statement at once rouse the thought that it is not surprising that the ovary, the mother and progenitor, possessing such tremendous potentialities for diversification of function and morphology, should also possess the faculty of having these same functions and morphology vitiated and therefore of diverting these potentialities into an equal number of abnormal growths?

In order fully to understand that statement, one must know something; yes, much, of the cell differentiation which takes place in the

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

ovary, but one must understand still more the tremendous powers of vicarious function possessed by each component cell of the ovary.

Embryologically the ovarian cells are derived from the mesenchyme. At first they are undifferentiated. They all appear to be alike. This stage of development is often spoken of, but probably wrongly so, as the asexual stage. It is too deep a subject, this subject of sex, to enter into here, but *en passant*, it is not known, as yet, whether all the specific cells of the ovary are capable of forfeiting their normal quota of genes to become ova, or whether ova are set apart at an early stage of embryonic life, and the number of these once fixed cannot be increased at a later date. Oogenesis certainly goes on throughout the life of certain lower animals, but perhaps these animals are still in the embryonic state relative to man's progress in evolution. It is certain, however, that a pseudo-oogenesis goes on in some of the higher vertebrates, as I described in one of my previous works. But whether any of these pseudoformations arising out of the fusion of several cells ever reach the stage of normal oogenesis is indeed not only problematical, but very doubtful. But at least this pseudo-oogenesis shows that the body of that animal must have undergone some metabolic change reverting it somewhat to the embryonic stage when oogenesis was a normal function. The importance of this finding in the lower vertebrates is important. It may have a direct bearing upon those complex tumors, such as dermoids and teratomas, that are characteristic of ovarian tissue and are looked upon as derived from totipotential cells, such as ova, in that these tumors may contain all or some of the somatic layers of the normal embryo.

The components of the adult ovary are made up of three types of cells that are specifically ovarian. They are:

1. The specific stroma cell.
2. The membrana granulosa cell.
3. The ova.

I have put them in this order because the two latter groups are descendants of the first one. The specific stroma cell lives a labile life. It has great potentialities and a versatility in mutation that is not equalled by any other single cell of the body corporate. And what is most important is that it retains this potentiality and versatility to a great degree throughout the human sexual life, though perhaps in a progressive diminuendo as sexual life passes its maturity. As to the stroma cell's function, this does not enter into the consideration of new growths, except that it is widely maintained that vitiated function invariably precedes vitiated and ungoverned cell division.

From these stroma cells there develops a form of new growth, a description of which has not yet been published. It is a local overgrowth of these cells with a thin capsule. They are akin to fibromas, but the component cells are distinctly those of specific ovarian stroma cells, similar in morphology to stromatous endometriomas. The majority of

these tumors are microscopic and benign, but malignant types have been found, though the malignancy is of low grade and does not metastasize until the tumor has reached large proportions. They are friable and vascular and closely resemble undifferentiated granulosa tumors.

The granulosa cell, a more highly developed stroma cell, by virtue of its elevation in the cell social scale, has acquired new functions and new growth properties. Its function is that of both morphologic and topographic subservience to the dominating influence of the ovum.

Among these cells we recognize three common forms of granulosa tumors, oophoromas, folliculomas, and morphologically undifferentiated granulosa cell tumors. These three differ only in degrees of higher functional loss. The oophoromas and folliculomas are never malignant, or if they are, their morphologic functional properties are lost, though we have no corroborative evidence that the transition ever takes place. Granulosa cell tumors are frequently malignant, though I must confess that it is one of the most difficult, most impossible, tasks to determine by microscopic study whether any given granulosa cell tumor is malignant or not. Many of them with all the clinical hallmarks of malignancy and with extensive peritoneal contamination at operation, and with microscopic characters that denoted malignancy, have run a clinical course for years which belied our best clinical and pathologic judgment. And per contra, others seemingly benign have run a most rapidly malignant clinical course. So far there seems to be no single or complex criterion upon which a wise prognosis can be based.

The co-existence of a granulosa cell tumor of the ovary and a carcinoma of the uterus, even in young girls, offers an interesting problem of cause and effect. There are those who contend, and with a great deal of justice, that hyperestrinism is the immediate cause of ovarian and pelvic new growths. It produces in susceptible tissue an urge to grow beyond the normal relations of tissues. This contention is further supported in a theoretical way by the close chemical similarity between estrin and carcinogenic substances. The influence of estrin in malignancy seems to be borne out in the coincidence of a granulosa cell tumor and a carcinoma of the endometrium. I have two such cases, one patient at 22 years and the other at 25 years of age. They were both cases of ovarian dystrophy and had been under observation and treatment for years. There can be very little doubt that the uterine malignancy was secondary to the granulosa because this coincidence has been recorded so often in literature as to transcend the laws of chance coincidence. And there is now also very little doubt that the primary cause of the granulosa cell tumor lay in an abnormal anterior pituitary stimulation.

Luteal cell tumors, of rare origin, have more an academic interest than a clinical significance.

The ovum, with its idiosyncrasy of individual genes, is in a class by itself. It is a totipotential cell, comparable in this respect to no other cell in the human or animal body. It has only the property of division in common with other cells, but even in this respect it is individualistic. Other cells when mature reproduce only their own kind. But in the matter of differentiation the ovum is unique. When one considers that it not only can reproduce all the cell complexes of the body, but also their complex functions and transmit genealogic individual idiosyncrasies, one finds oneself in awe before a great mystery. The infinitesimally small and the infinitely great are the two extremes of which man, in his present mental development, cannot form any adequate conception. We do know, however, that the more highly an organism or machine is specialized, the more prone it is to easy upsets. It is also known from comparative physiology that quite a large percentage of ova are abnormal, either *ab initio*, or in the process of development.

From these two premises, and owing to the diversity of cell morphology usually found in dermoids and teratomas, it is generally agreed that these two forms of new growth are the expression of a vitiated metabolism upon ova. We have seen that in the lower vertebrates oogenesis may continue through the early years of sex maturity, and I have demonstrated in an old bitch that pseudo-oogenesis can and does take place. When we realize that parthenogenesis can be produced under experimental change of environment, we have in all these potent premises, factual evidence, or the conclusion that dermoids and teratomas are the result of vitiated growth in an abnormal ovum, *in situ*. Dermoids and teratomas are specifically female or male sex-organ tumors, and are found only in ovarian or testicular tissue, whether this be normally or ectopically placed. Therefore we can contend that dermoids and teratomas, being specific to ovaries, must arise out of cells that are specific to that sex organ, and consequently must arise out of ova or its progenitors. When, however, we come to the large class of pseudomucinous cysts, which are always potentially malignant, there is not such uniformity of opinion.

Many eminent pathologists claim that just as dermoids and teratoid growths are of oval origin, so pseudomucinous cysts are of the same nature and are composed almost exclusively of the endodermic layer, in the same manner as dermoids are composed almost exclusively of the ectodermic layer, and teratomas of all three component layers of the somatic body. Be that as it may, there is much to justify this opinion, and pseudomucinous cysts compose the foundation of most of the malignant papilliferous cysts of the ovary.

It is well to point out at this juncture that the popular belief is that a new growth may be benign for a long period and then, due to a change in circumstances, it may pass into a state of "malignant degeneration," meaning by this that the whole or a great part of that benign tumor may

undergo this malignant change in a large part of its substance. This is the concept that is expressed in the terms malignant degeneration of fibroids, malignant degeneration of ovarian tumors. According to the present concepts of malignancy nothing could be farther from the truth. We now believe that malignancy is usually the property of a single cell, and that all malignant cells of a tumor are derivatives of that parent cell. So if a tumor is malignant it is so from its inception, or, under the urge of growth of any tumor, a single cell of that tumor may become malignant owing to a change of circumstances in that growth. The second above-mentioned malignant change in an otherwise benign new growth is much the rarer condition, in fact, very rare condition. Something more, however, must be borne in mind. Malignant tumors have a tempo of growth, that may vary within wide limits, and in any battle between tumor and host the tempo will change according to the changes of resistance of the host. In this respect malignant new growths run a course parallel with that of infections, but in malignancy the victory is always a foregone conclusion unless some remedial measure, natural or artificial, enters to upset that certainty. The tempo of a growth, as was stated, may vary within very wide limits, and when the tempo is reduced to that approximating nonmalignant growths we may reach the no man's land between malignancy and nonmalignancy. Let us not forget in our speculation that a new growth is malignant or nonmalignant from its inception, and that the variance in opinions of pathologists is merely due to our lack of knowledge of determining factors.

Malignancy may be summarized as follows:

1. The morphology of the cell composing the growth depends upon the organ from which it primarily arose.
2. The tempo of the growth depends upon the terrain and the acquired or inherited corporeal lack of resistance.
3. The rapidity of extensions and remote metastases depends upon the size of the individual new growth cells and the host's resistance.

With few exceptions ovarian malignant new growths possess a slow tempo and metastasize remotely quite rarely, and that quite late in the disease.

Another problem of new growths is to determine what causes one new growth to grow as a malignant papilloma while another grows as an infiltrating carcinoma. Some tumors combine both forms of development. It is now maintained that these two forms of extension are the same, except that the papilliferous types require a cavity (either cystic or peritoneal) for development corresponding to foliage, whereas the carcinomatous type of extension requires a supporting structure of solid tissue, corresponding to roots and earth, respectively. And just as in botany, the aerial and terrestrial are to a degree interchangeable, so it is also with malignant new growths.

The origin of the simple serous cysts of the ovary is a subject of dispute, but as these are never malignant they do not enter into this study.

The arrhenomas are in a class by themselves. Their origin is no longer a matter of dispute. In my former writings, I pointed out that woman as regards her ovaries is in a higher rank from a point of view of evolution than is man. Her ovary passed through the testicular stage of development on to the ovarian stage. The old embryologic law still holds good, that what is permanent in the lower types is transitory in the higher. In passing through the lower testicular stage to the higher, certain ovaries retain some traces of the lower male order, and under certain conditions of metabolic environment these dormant atavistic structures are lighted into activity, not only morphologic but often functional activity. Interesting as are these tumors from an evolutionary and embryologic standpoint, they are not germane to our subject as they are rarely malignant.

CLINICAL CONSIDERATIONS OF OVARIAN MALIGNANCIES

Modes of extension of malignant ovarian growths. It is generally conceded that ovarian malignancies extend almost exclusively by one of two methods.

1. By direct contamination of the peritoneal cavity by a process of implantation.
2. By lymphatic progress.

1. It is important to realize that nearly all malignant growths of the ovary begin in the medulla of the ovary. I have found malignancy of the ovary so small as to be microscopic, yet always deep in the substance of the ovarian stroma. The tunica of the ovary offers a substantial barrier to its outward progress for a considerable period of time, depending upon the tempo of the growth. Knowing this, we are always hopeful that by removing such ovaries in toto, the further extension of the disease may be circumvented. Whether the malignancy is of the papilliferous type or of the carcinomatous variety, the clinician, having no authority over the growth, hopes to intervene before the ovarian capsule has been overcome. Contamination of the peritoneal cavity takes place by one of two methods: in the malignant papilliferous cysts, the papillas gradually encroach upon the fluid content and then expand the capsule to the point of rupture. The further progress is by peritoneal implantation upon tissues that become soiled by the grafts. The opposite ovary, if not involved simultaneously in malignancy, may develop implants upon its surface, and become densely adherent in the depth of the pouch of Douglas. The ovary which is primarily affected usually has reached a considerable size before fixation takes place, and during this interval it was free to rise in the abdomen, and usually

became extrapelvic in its lie before becoming fixed by adhesions. Carcinomatous growths are usually solid and reach the peritoneal cavity by direct extension. Malignancy, however, seems often to develop in both ovaries simultaneously and independently.

2. Metastases from ovarian malignancy propagated through the blood stream are extremely rare.

Progress along the lymphatic chains and nodes, however, is extremely common, but fortunately is a late development. Ovarian malignant tumors have a relatively long period of local activity. In this respect they differ from malignancy of other organs, such as stomach, breast, etc. Even progress along the lymphatics is slow, and remote metastases are a very late development. The one notable exception to this rule is found in the rapidly growing and metastasizing granulosa-celled tumors. They fortunately are rare.

The one great hope for the surgical clinicians lies in attacking the malady in its local stage before its extensions have occurred.

To clinicians three problems at once suggest themselves.

1. Can we distinguish a malignant from a simple ovarian growth.
2. Should we endeavor to remove the primary growth when extension to neighboring structures has occurred.
3. In all cases of suspected malignancy should one remove both ovaries whether the second be visibly affected or not.

1. So far as I know there is no clinical criterion by which one can distinguish a nonmalignant from a malignant ovarian growth. Especially is this true while the malignant growth is still limited to the ovary and encapsulated. Yet this is the only period in which malignancy can be dealt with satisfactorily. Ovarian new growths are unfortunately singularly free from symptoms. Even the menstrual cycles and characters are seldom disturbed.

The advent of pain, or of free fluid in the abdomen are too often the heralds of ineradicable extensions. As previously stated ovarian malignant growths are usually slow in development. Their tempo is usually considerably less than similar growths elsewhere. This allows a long period during which the disease is purely local and offers greater chances of a hopeful complete eradication of the disease. It is unfortunate that ovarian new growth is so symptom free. So many patients consult us merely because the abdomen is enlarging. So pronounced is this freedom that many spinsters with a guilty conscience and married women come because pregnancy is suspected, owing to the abdominal enlargement. It is pathetic, however, how many cases come under observation only when the disease is too far advanced to permit any chance of total eradication.

2. When dealing with a known malignant tumor at operation, one can usually judge after a rapid survey of the abdominal cavity whether the growth is removable or not. In removing an encapsulated growth

it is often desirable to do so through as small an incision as possible by aspirating the growth and removing its contents, thereby permitting the collapsed capsule to be withdrawn through a very small opening. It is not always possible to distinguish the character of cysts by inspection, and for fear that a suspected simple cyst may eventually turn out to be multilocular, within a smooth uniformly dense capsule, exploratory perforation of the cyst by a trocar should be done very cautiously for fear of peritoneal contamination. When the mistake has been discovered, it is not always possible, in fact, rarely possible, to close the trocar puncture satisfactorily to avoid contamination during the extension of the incision and the enucleation en bloc.

When, however, upon opening the abdomen, the case presents a definite peritoneal involvement, I know of no rule which can be laid down to guide the surgeon. Only experience can be a safe judge. In these circumstances both ovaries are generally involved, one higher up, and the other bound down by peritoneal extensions in the pouch of Douglas. When, however, the ovarian growths can be removed without too much risk, even at the expense of considerable difficulty, it is thought that the period of life is lengthened. This is a debatable point, for no one can state what the tempo of that tumor was before operation, and what will be its rate of growth afterward. I have had a patient who had both ovaries removed for malignant growth, the tumors were the size of coconuts, and the retroperitoneal glands were the size of walnuts, yet she lived eight years with apparently normal health, only to die of metastasis in the end. Others seem to progress at a faster tempo after surgical intervention.

3. It is my policy to remove both ovaries whenever there is undoubted malignancy of one of them. This is not so radical a procedure as one might suspect. Most of these patients are in their late thirties or older, and spaying, as a rule, does not involve any grave consequences. In the young girl, however, the problem becomes a sentimental question. Granulosa cell tumors are notably found in the young. In two of my cases the patients were 22 and 25 years of age. I removed both ovaries, yet I know now that malignancy in granulosa tumors is difficult to define even with the microscope, though granulosa cell tumors are easily recognizable by their striking characters. Under these circumstances we would doubtless be radical in many cases and not feel any remorse.

It would seem that deep x-ray application should find in malignant ovarian disease a field of great usefulness. But, my experience is at variance with that of others, because I have found deep x-ray therapy singularly inefficient in the cure or alleviation of cases of peritoneal involvement. It is my conviction that x-rays not only do not improve, but have almost invariably broken down the patient's health and hastened death. This untoward result cannot be attributed to the roentgenologists, because these are highly trained men in various hospitals of

the city of Montreal, where instruments of high potency are at their command. So we are forced to the conclusion that the only hope for a patient suffering from incipient malignancy of the ovaries lies in early extirpation, before the disease has spread beyond the confines of the ovary. This will necessitate exploratory operation upon any suspicious tumor of the ovaries. Our attitude toward ovarian new growths must be somewhat akin to the position we adopt toward tumors of the breast. Doubtless many abdomens will be opened needlessly. So it should be our endeavor to make exploratory celiotomy free from unexpected accidents by careful preoperative study of the patients, so that eventually this operation can be recommended without fear of untoward complications. The long period of confinement of the disease of the ovary gives a wider margin of cures. But the paucity of symptoms in local new growth militates strongly against the patient, in that consultation is frequently deferred beyond the period when the disease is solely ovarian.

1472 SHERBROOKE STREET, W.

DISCUSSION

DR. VIRGIL S. COUNSELLER, ROCHESTER, MINN.—In general, in all cases in which there is a tumor of one ovary, and the other ovary is normal, I advise removal of the diseased ovary. If however, there is a suggestion that both ovaries are involved I advise removal of both ovaries, the uterus, and tubes. In the presence of operable papillary ovarian cysts, panhysterectomy should be performed because implants are likely to occur in the uterus and tubes. Since the condition is often bilateral, in the case of any carcinomatous ovary either cystic or solid, I propose panhysterectomy.

I cannot agree with Dr. Goodall in his statement that these pelvic malignant growths are slow in development and metastasize late. It has been my experience and that of my colleagues that there are four different types of growth according to the grade of malignancy (Broder's classification). Those of low malignancy do grow slowly and extend late, but unfortunately many of these growths are of the high grade of malignancy, Grade 3 or 4. This is particularly true of the solid ovarian cancers. On the other hand a malignant lesion of high grade that is still intracystic is favorable for surgical cure.

At the Mayo Clinic we feel that any patient beyond the age of 37 years who has an ovarian cyst of fair size should be subjected to exploration, because the chance that these cysts are malignant increases progressively beyond this period in life. I believe that clinically it is possible to suspect malignant cysts on bimanual examination because the cyst is tense and gives the impression of being heavier than the ordinary simple cyst. It may have one or two attachments in the pelvis.

As to treatment, I am in agreement with Dr. Goodall with regard to roentgen therapy. The longer I am able to follow these cases the more I doubt the value of roentgen therapy. I believe that whenever it is possible to remove the affected organs, even though there may be some metastasis to the omentum, the patient will live just as long without roentgen therapy as with it. At the Mayo Clinic we have records of patients living twenty-five years following panhysterectomy for malignant cysts with metastasis. For some reason secondary growths in some cases regress or fail to progress following removal of the parent structure.

DR. EMIL NOVAK, BALTIMORE, Md.—Dr. Goodall's plan of subdividing granulosa cell tumors is unorthodox and seems to me unwise. For example, he applies to one group the designation of oophoroma, a term which until recently was commonly applied to a totally unrelated family of tumors, those of Brenner type. The so-called oophoroma folliculare of former years is now quite universally spoken of under the eponymic designation of Brenner tumor, and it is totally different histologically and histogenetically from the granulosa cell tumors.

I agree with Dr. Goodall as to the impossibility of prognosticating the degree of clinical malignancy of granulosa cell carcinoma on the basis of histologic criteria. The tumors which occur in prepuberal patients have seemed to be less malignant than those occurring during reproductive life, but this may be due to the fact that the striking biologic effects produced by such tumors in children, comprising the syndrome of precocious puberty, bring them to medical attention much earlier than when such tumors occur during reproductive life, when such biologic effects are not seen.

There is still some difference of opinion as to whether the cystic forms of ovarian carcinoma are always secondary to benign cystadenoma or whether they may represent carcinoma *ab initio*. There is certainly no question that cancer frequently develops in previously benign cystadenoma. Most of us have seen patients in whom large cysts have been known to be present for many years, and in whom later removal of the cysts has shown definite cancer developing in the wall of the cysts. A not uncommon observation in all laboratories is to find cancer only in a localized area of an otherwise benign cystadenoma.

From a practical standpoint, if the surgeon at operation encounters a cyst which is thin-walled throughout, it is reasonably certain to be benign, and conservative operation is indicated. If, on the other hand, a hard indurated mass is felt at some portion of the cyst, the surgeon's suspicion should be aroused, and certainly the cyst should be opened before the abdomen is closed, as this will often give additional naked eye information. If a serous cystadenoma presents only a few papillomatous outgrowths on its surface or within its cavity, it is most likely to be histologically benign, but if it is filled with a mass of necrotic papillomatous growth, it is reasonably sure to be malignant, and radical surgery is indicated. These are broad generalizations, and exceptions are of course encountered, but they demonstrate the importance to a surgeon of a knowledge of pathology. This is of much greater practical value than the collaboration of a pathologist *confrere*.

With reference to the management of granulosa cell tumors, those seen in children should in general be treated conservatively, and those in reproductive or postmenopausal life radically, with individual exceptions based on such factors as age and the importance or unimportance of later pregnancies. Dr. Goodall certainly need not apologize for advocating removal of both ovaries in cases of unilateral ovarian carcinoma. Not only the ovaries but also the uterus should be removed in view of the frequency of extension to the latter organ. To do less would in the ordinary case of ovarian carcinoma be culpable, unless technical difficulties make this impossible or inadvisable.

As to postoperative radiation, its advantages are difficult to evaluate, but most of us will employ it simply to make sure that nothing of possible benefit to the patient is omitted. I do not believe, however, that it is very often of decisive value.

Finally, I should like to emphasize the inadvisability of operating on very small cysts. Many of these are of nonneoplastic, i.e., follicle or corpus luteum type, and they are of transient nature. All of you have found that at subsequent examination cysts, as large as a lemon or small orange, have completely disappeared. On the other hand, in the definitely neoplastic variety, operation is ordinarily advisable even in the absence of symptoms, not only because of the frequent occurrence of such

complications as torsion of the pedicle, but even more because of the malignant potentialities of ovarian growths, much greater, for example, than pertain to uterine myomas.

DR. JAMES K. QUIGLEY, ROCHESTER, N. Y.—I should like to report an example of the rapidity of growth of a malignant ovarian tumor. The patient, a woman of 60 years, was curetted for bleeding in December, at which time no enlargement of either adnexa was noted. A month later she had an ovarian growth the size of an English walnut, and four months later it had developed into an orange-sized tumor, at operation no metastases were discoverable, but both ovaries were removed, and radiation given. Should this postoperative radiation have been used?

DR. JOE V. MEIGS, BOSTON, MASS.—When one discovers a tumor of the ovary, if it shows papillomatous growth inside or out, one should consider doing radical surgery. All ovarian tumors can metastasize to the uterus and thence to the cervix, and I believe, therefore, that total extirpation of the uterus plus removal of both tubes and ovaries should be done. In our own series about 40 per cent of all ovarian tumors were bilateral and for that reason I think there is some predisposing anatomic or histologic abnormality. The chances are that if one ovary is involved the other probably is also.

A very small percentage of patients with solid carcinoma of the ovary live five years following operation, but 23 per cent with malignant papillary cystadenomas do live. Patients having x-ray treatment do not survive in any greater numbers than those that do not have such treatment. Nevertheless, in our series life was lengthened about three months in those who had x-ray treatment. I have some patients who are still alive who had x-ray treatment for inoperable cancer and were operated upon radically later.

One word may be said about another tumor, namely the fibroma of the ovary with fluid in the abdomen and chest. One usually assumes that such fluid is due to metastasis from cancer and that therefore no surgery should be undertaken, yet in the last year we have had 3 patients with fibroma of the ovary with pleural fluid. Patients whom we might regard as hopeless because the chest and abdomen are full of fluid should not be condemned until this syndrome has been excluded. Twenty-six such cases have now been reported, and it is certain that there are many other patients who are being overlooked.

DR. GOODALL (closing).—Of course, it is well known that fibromas of the ovary usually are associated with fluid in the chest and ascites. In patients with such accumulation of fluid in the presence of an ovarian tumor, it is often difficult to determine whether we are dealing with a simple fibroma or a malignant growth. This uncertainty is often a reason for operating.

I would not presume to answer definitely Dr. Quigley's question of whether x-ray was rightly or wrongly used in his case, but the fact that the tumor was malignant would probably have caused us to use x-ray, at least as a salve to our conscience.

With regard to the oophoromas, there was a slight misunderstanding between Dr. Novak and myself. According to my view it is a small tumor which grows slowly but which still retains some of the function of the stroma cells.

HYSTERECTOMY IN PREGNANCY, LABOR, AND THE PUERPERIUM*

GERALD W. GUSTAFSON, M.D., F.A.C.S., INDIANAPOLIS, IND.

(From the Department of Obstetrics, Indiana University School of Medicine)

THERE is a small but definite place in the field of obstetrics, for hysterectomy. Probably no other operation so clearly demonstrates the justification for unity in obstetrics and gynecology. This paper is an attempt to correlate the indications for hysterectomy in pregnancy, labor, and the puerperium, and is based on those hysterectomies done on the obstetric service of the William H. Coleman Hospital, and the personal experience of the author. This discussion will be limited to abdominal hysterectomy, as aside from an occasional inversion of the uterus, there is little indication for vaginal hysterectomy in obstetrics.

From the opening of the Coleman Hospital in October, 1927, to Jan. 1, 1941, there have been 12,536 deliveries including all births of babies of 1,000 Gm. or more. During this period there have been 27 abdominal hysterectomies definitely associated with the parturient state.

HYSTERECTOMY DURING PREGNANCY

Tables I and II include those patients on whom hysterectomy was performed during pregnancy; Table I being those cases before viability, and Table II those past viability.

HYDATID MOLE AND CHORIONEPITHELIOMA

While chorionepithelioma may occur after abortion or labor, at least 50 per cent of chorionepitheliomas follow hydatid mole. All authorities seem agreed upon two facts, namely: (1) that hysterectomy is not a routine necessity after hydatid mole expulsion or removal; and (2) that in the presence of chorionepithelioma, panhysterectomy followed by radiation is indicated. Our great problem then is to watch patients that have had hydatid mole so that early chorionepithelioma may be discovered. I am not in agreement with those who advise the removal of hydatid mole by hysterotomy so that the interior of the uterus may be examined for evidence of invasion. In my own case, C-12875, most of the lesion was in the wall of the uterus, and an incision in the anterior wall of the uterus might easily have missed the lesion. The hydatid may be removed by sponge forceps from below and the case watched by repeated Aschheim-Zondek or Friedman tests. If the test

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

TABLE I. HYSTERECTOMY ASSOCIATED WITH PREGNANCY (BEFORE VIABILITY)

	INDICATION	NUMBER	DATE	AGE	PARITY	MORBIDITY	MORTALITY	FETAL MORTALITY	REMARKS
1	Suspected chorionepithelioma (syncytial endometritis)	XC-27559	12/16/38	24	i	Yes	0	No	Syncytial endometritis
2	Chorionepithelioma	3162	5/ 1/29	28	v	Yes	0	No	No follow-up
3	Chorionepithelioma	C-12875	7/19/37	32	v	No	0	No	4-year cure
4	Interruption of pregnancy and sterilization	9600	8/20/31	34	i	No	0	Yes, 3 mo.	Tuberculosis
5	Toxemia, syphilis, and abruptio placentae	C-8841	10/ 9/35	19	i	Yes	0	Yes, 6 mo.	Hemorrhage into uterine wall
6	Interruption of pregnancy (carcinoma of cervix)	XC-47930	2/20/41	28	i Gravida iii	Yes	0	Yes, 4½ mo.	Later radiation
7	Fibroid uterus	3414	6/19/29	30	i	No	0	2 mo.	Pain in side and 3 large fibroids
8	Fibroid uterus, general debility and extreme fatigue	184	11/25/27	33	xii	No	0	Yes, 2 mo. fetus	Did laparotomy for interruption of pregnancy
9	Huge fibroids, spontaneous abortion and retained placenta	XC-42119	8/28/40	46	Gr. iii	Yes	0	Yes, 5 mo. fetus	Uterus at 5 months to xiphoid
10	Ectopic pregnancy	XC-34122	11/27/39	28	Gr. ii	Yes	0	4 mo. fetus	Ruptured into broad ligament

TABLE II. HYSTERECTOMY ASSOCIATED WITH PREGNANCY (AFTER VIABILITY)

	INDICATION	NUMBER	DATE	AGE	PARITY	MORBIDITY	MORTALITY	FETAL MORTALITY	REMARKS
11	Rupture of uterus	10159	10/23/31	20	iii	Yes	0	Yes	At 7 mo., 1 previous normal delivery, and 1 classic section
12	Rupture of uterus	C-7890	12/ 2/36	23	iii	Yes	0	Yes	7 mo. 2 previous sections (classic)
13	Large fibroid	7132	11/ 1/30	35	i	No	0	0	Baby 7-6, uterus and fibroid 6-7
14	Fibroid uterus	C-7803	7/20/35	36	i, Gr. ii	No	0	0	Degenerated necrotic fibroid
15	Post cesarean ventral hernia	XC-31473	12/20/39	26	v	No	0	0	1 previous cesarean section
16	Carcinoma of cervix	C-14246	2/ 4/38	37	ix 8 living children	No Died 1 year later	0	0 Neonatal	8 mo. gestation
17	Carcinoma of cervix	XC-49980		36	vi	0	0	0	7½ months gestation
18	Cervical stenosis (following cauterization)	C-4966	3/21/41	23	ii	No	0	0	Previous classic section and removal of cervical polyps by deep cauterization
19	Abruptio placentae and toxemia	XC-24504	9/17/38	24	i	0	0	Yes	Toxemia apparently improved shortly before abruptio placentae

remains positive for three months and there is in addition *definite retardation of involution* with or without bleeding, the question of hysterectomy must be given grave consideration. Under such circumstances I would advise hysterectomy, particularly if the woman had several babies, even if curettings showed no evidence of malignancy.

Schumann recently stated as follows: "Radical surgery is indicated whenever persistent fetal elements are present, especially if irregular bleeding is a symptom, regardless of a negative Aschheim-Zondek test."

While the Friedman test is helpful, it is many times confusing because a normal pregnancy may show large quantities of gonadotropic hormone. Also chorionepithelioma may be present and the patient show only a weakly positive or even a negative test.

In our series, hysterectomy was performed three times with a tentative diagnosis of chorionepithelioma, in patients who previously had had moles. In one the pathologist's report was syncytial endometritis. In another, the report was chorionepithelioma, but there was no follow-up. The third case was the author's, occurring in the presence of a weakly positive Friedman test. Complete hysterectomy, including removal of both tubes and bilateral luteal cysts, has been followed by a four-year cure. In the 15 Philadelphia cases, Schumann reported two cases cured by panhysterectomy. It is the obstetrician's opportunity to diagnose this type of malignancy in its early stage and undue procrastination may seal the doom of his patient.

INTERRUPTION OF PREGNANCY AND STERILIZATION

In this hospital, hysterotomy and sterilization has been much more popular than hysterectomy, as 44 hysterotomies were performed for this indication. Particularly in the older group of women, I believe hysterectomy to be the preferable operation. It can be done as quickly, with less blood loss and patients have a smoother convalescence. Certainly one feels more certain of sterilization than after any type of tubal ligation or excision. It is of interest to note that the only case of abdominal wound endometrial transplant that this author has had develop, was after a hysterotomy and sterilization.

The chief objection to hysterectomy, namely, that the fundus has definite endocrine functions, has not been proved. In carcinoma of the cervix in early pregnancy, if abdominal termination is selected before radiation, supracervical hysterectomy would seem much safer than hysterotomy in the presence of the secondary infection. In this series, one case of carcinoma of the cervix was interrupted before viability by hysterectomy, as were two cases after viability. We are in agreement with Danforth who urges Porro section in those women who have carcinoma of the cervix discovered after viability. If these patients are delivered by conservative section, an occasional patient will be lost from infection.

FIBROMYOMA OF THE UTERUS

Rarely is it necessary to remove a fibroid uterus during pregnancy. However, Campbell has shown that the relation of degeneration in myomas in pregnant to nonpregnant uteri is about 9 to 1. If there is very rapid growth or degeneration characterized by pain, leucocytosis, fever, and softening of a subserous fibroid, myomectomy is occasionally warranted. In the case of torsion of a pedunculated fibroid, this operative procedure can be safely and easily performed.

Hysterectomy was done on three cases in this series.

One patient (C-3414) had a large fibroid uterus the size of a six months' pregnancy, at two months, and complained of constant severe pain. Another (C-184) was a para xii with general debility and exhaustion, and the decision to interfere was probably influenced by this fact. The third patient is the only one upon whom I have performed hysterectomy for fibroid uterus during pregnancy, and this was after expulsion of the fetus. This patient had had two spontaneous abortions, was 46 years of age, and very anxious for a child. We attempted to carry her through, but she entered the hospital and aborted a fetus at five months. At this time the uterus was to the xiphoid. The placenta was retained. First an incision through the anterior wall of the uterus was made, the placenta separated, and delivered by an assistant from below by traction on the cord, and then a subtotal hysterectomy was done. Another patient had a hysterectomy done after section at term because of a degenerating fibroid, and another was operated upon for a large fibroid which blocked the birth canal.

Huber and Hesseltine recently have called attention to the danger of myomectomy done at the time of cesarean section. This operation was done once at this institution and the mother died of peritonitis.

ABRUPTIO PLACENTAE

It is occasionally necessary to do hysterectomy in the very severe cases of abruptio placentae. The one patient operated upon during pregnancy was a nephritic patient who had superimposed toxemia. This toxemia had greatly improved on hospital management, and the patient was sent home. Two weeks later she entered the hospital with severe intra-uterine hemorrhage, a boardlike abdomen, and with no fetal heart tones. Hysterectomy was done as there was extensive hemorrhage into the uterine wall.

Whenever a severe abruptio placentae is admitted, transfusions are usually indicated. While operation is sometimes necessary, I have been amazed with the excellent results of conservative treatment as advocated by De Normandie, Irving, and others. With rupture of the membranes, a small dose of pituitrin and the application of a Spanish windlass, many of these patients will go into labor. Certainly this treatment is deserving of a trial before operation is resorted to. The crux of the matter seems to be whether or not the uterus can be stimulated to contract.

MISCELLANEOUS INDICATIONS DURING PREGNANCY

The patient who had hysterectomy following section at term, because of a large ventral hernia, was one who had a previous section followed by herniation of the uterus through the recti. At the time of this second operation the herniation was so great that the incision in the uterus was in the posterior wall. As the abdominal wall was of almost paper thinness, it was thought advisable to remove the uterus.

Another patient was subjected to hysterectomy at the time she was operated upon for an ectopic pregnancy of four months, that had ruptured into the broad ligament. It was felt that better peritonization could be accomplished by hysterectomy.

RUPTURE OF THE UTERUS DURING PREGNANCY

The large number of women who have had cesarean section are subject to this real danger throughout a following pregnancy. In this series there were three patients all at about seven months' gestation, who entered the hospital with rupture of the uterus. All had previous classic cesarean sections. Two had not been in labor and one had had four hours of labor. Fortunately all had an early diagnosis, a hysterectomy, and all recovered. In another case there was a small opening in the old incision so the scar was freshened and the uterus left undisturbed.

He who is faced with the decision for an initial cesarean section must take into consideration the possibility of rupture in a following pregnancy. If there was no other advantage of the low cervical over the classic operation than the increased protection against rupture of the uterus in a following pregnancy, I would select the former.

HYSTERECTOMY DURING LABOR

In addition to the patient previously mentioned who had a rupture of the uterus develop after four hours of labor, there were two traumatic ruptures occurring during labor.

The first had had attempted forceps in the home and then three ampoules of pituitrin. The second patient was a para xii with a transverse position. Our resident felt the uterus rupture while attempting to loosen the shoulder girdle. Immediate hysterectomy and transfusions were life saving in these cases.

The one case of fibroid blocking the birth canal was operated upon before labor but in case of doubt there is every reason to give such a patient a trial labor. No case of abruptio placentae or placenta previa in labor was subjected to hysterectomy.

A para vii was subjected to cesarean section plus hysterectomy after she had been in hard active labor many hours with failure of a scarred cervix to dilate.

TABLE III. HYSTERECTOMY ASSOCIATED WITH LABOR

	INDICATION	NUMBER	DATE	AGE	PARITY	MORBIDITY	MORTALITY	FETAL MORTALITY	REMARKS
20	Rupture of uterus	5471	4/ 6/30	27	iii	No	0	Yes	4 hours' labor. Previous classic section
21	Traumatic rupture of uterus	C-6033	8/10/34	27	iv	Yes	0	Yes	3 previous normal deliveries. 12 vaginal examinations in home. Forceps attempt for two hours. 3 ampoules pituitrin
22	Traumatic rupture of uterus	C-12232	2/ 6/37	42	xi	Yes	0	Yes	Transverse position. Uterus ruptured while attempt at version was being made
23	Cervical dystocia	C-14060	10/16/37	43	vii	0	No	No	Long labor

TABLE IV. HYSTERECTOMY ASSOCIATED WITH THE PUERPERIUM

	INDICATION	NUMBER	DATE	AGE	PARITY	MORBIDITY	MORTALITY	FETAL MORTALITY	REMARKS
24	Necrosis of fibroid	XC-35438	5/22/40	32	ii	Yes	0	0	6 weeks after precipitate delivery
25	Infected fibroid	2993	5/ 1/29	36	ix	Yes	0	0	Transverse position delivered by version
26	For sterilization; vascular renal disease and recurrent toxemia	XCL-25740	7/19/40	24	Gr. ii	0	0	Yes	Delivered macerated fetuses on Oct. 10, 1938, and June 29, 1940
27	For sterilization nephritis and recurrent toxemia	C-4188	8/17/36	32	P.v	Yes	0	No	Toxemia in 3 pregnancies. Eclampsia in one

CESAREAN SECTION IN THE INFECTED PATIENT

We have all seen cases which have been mishandled in labor with otherwise absolute indications for cesarean section. Not always is the baby dying, and it is only human that we should shrink from craniotomy. The recent publication of a new and ingenious technique of extraperitoneal cesarean section by Waters has added much interest to this problem. If the spill is the major thing in the production of peritonitis in cesarean section, then our problem is solved by extraperitoneal operation. Waters states as follows: "Cesarean hysterectomy can not conceivably be better than a true extra peritoneal operation except in the 15 to 20 per cent group of fatal sepsis through uterine wall and lymphatics, and even in this group one may question its effectiveness." My own conception of this problem has been stated in a previous paper. I am convinced that the spill is not the greatest factor in the production of peritonitis. In two women dying from postcesarean peritonitis at this Institution, autopsy showed infection and necrosis in the uterine incision. The peritoneum will usually stand one severe insult but with repeated insults from an infected uterine incision in the peritoneal cavity, peritonitis is likely to occur. In other words, a uterine incision in the peritoneal cavity is most dangerous in these cases. The low segment incision completely covered with visceral peritoneum is safer. In comparing this operation with the extraperitoneal, it would seem only just to include drainage of the retrovesical space as Waters does in his operation. Safest of all, though sacrificing the uterus, would seem to be cesarean section plus hysterectomy, as only the cervical stump incision is left to suppurate, the large infected organ is removed, and the uterine vessels ligated. The publication of more necropsy material in failures of the various types of operation, will do much to clarify this problem.

HYSTERECTOMY ASSOCIATED WITH THE PUERPERIUM

An infected degenerated fibroid may be an indication for hysterectomy during the puerperium. One patient in this series was delivered by version and extraction because of transverse position. She had a large fibroid, and the puerperium was characterized by fever and subinvolution. Hysterectomy was done nineteen days after delivery. A second patient was operated upon six weeks after delivery. The author has had one case where a submucous fibroid was delivered through the cervix after the patient had returned home from the hospital. This was removed from below by means of the cautery. Two patients were operated upon for purpose of sterilization on the fifteenth day of the puerperium because of malignant hypertension and recurrent toxemia.

Autopsy on one patient, dying shortly after delivery from hemorrhage, revealed an undiagnosed submucous fibroid and a partial placenta accreta. One other patient with partial placenta accreta was treated by manual removal.

In connection with the puerperium, an unusual case of placenta spuria accreta, or partial accreta, is worthy of comment. The author did a transverse cervical cesarean on this patient (G-12097) at St. Vincent's Hospital, Nov. 15, 1937, because of a large baby with frank breech presentation and a small justo minor pelvis. The placenta presented through the incision and was delivered by slight traction. It seemed to be complete and was also reported so by the pathologic laboratory. On the twelfth postoperative day, preceded by nine days of normal temperature, the patient had rather profuse hemorrhage and pulse was elevated to 100. She was transfused and went home on the twenty-second day apparently in excellent condition with a red count of 3.4 million and a hemoglobin of 70 per cent. Four days later, at home, she suddenly had another profuse hemorrhage and was returned to the hospital. Upon admission she was still bleeding and was very anemic. She was taken to surgery where the cervix was found dilated to about 3 or 4 cm. Blood clots were removed from the uterus and tissue attached to the anterior wall could be felt with a sponge forceps. The tissue could not be removed but two or three small pieces were pulled away and found to be placental tissue when examined at the laboratory. The uterus was tightly packed. The next day the patient had a chill and temperature rise to 104° F. With a diagnosis of placenta accreta, a subtotal hysterectomy was done and the packing not disturbed until the uterine arteries were clamped, after which it was removed from below. The patient was transfused twice and recovered after some five days of temperature elevation.

The gross pathology showed a uterus of 100 mm. in diameter. There was adherent placental tissue in the upper right hand corner of the cavity of the fundus, 50 mm. long, 50 mm. wide, and 20 mm. thick. Chorionic villi seemed to dip down into the uterine muscle with absence or marked degeneration of decidua basalis. The tissue and gross specimen was submitted to a second pathologist, who concurred in the diagnosis.

THE VALUE OF INTRAUTERINE EXAMINATION AT THE TIME OF CESAREAN SECTION

Because of the experience of the above case, I determined to make it a point to explore thoroughly the uterus at the time of cesarean section. Little is stated in textbooks on obstetrics, about the conduct of the placental stage at the time of cesarean section, except that the uterus should be wiped free from membranes. In the classic section, the fundus is usually open for a clear view but in a low cervical operation the fundus is a cavity opened at the lower end, usually inaccessible to visualization. Yet there is always the possibility of abnormal placental attachment, the presence of a submucous fibroid or of injury to the uterus. Further justification of this procedure was emphasized to me by the following case.

Case Report.—E. M., a primipara, with an android type pelvis of the dystocia dystrophia syndrome type, had sharp pains in the epigastrium which doubled her over, after lifting a heavy piece of coal to the furnace.

She had continuous pain the remainder of the day. Her pulse and fetal heart tones were within normal limits. Pain continued and she entered the Methodist Hospital early the next morning in active labor. At 3 P.M. the patient had complete dilatation but station was -2, and there was marked overriding of the head with membranes having been ruptured for about six hours.

I did a transverse cervical cesarean; the baby was delivered and cried immediately. However, a swelling of one hip was present. The placenta was removed and exploration of the fundus revealed a large rupture of the roof of the uterus through which the hip had formed a perfect tampon. Some old blood was found in the upper abdomen. Immediate hysterectomy was followed by an uneventful recovery, the patient having no morbidity in the puerperium.

The rupture could easily have missed detection and the lower segment section completed. Hysterectomy was in my opinion definitely indicated.

Routine packing of the uterus, with the lower end of the pack attached to a shuttle of the DeLee type and placed through the cervix, will obviously reveal any marked stenosis of the cervix. Coleman's case (C-4966) was a patient who had had a previous section and some months before the present pregnancy she had had a very deep cauterization for cervical polyps and endocervicitis. At the time of this section I was unable to find an opening in the cervix and after the transverse cervical section, did a hysterectomy which was followed by the usual smooth convalescence. Phaneuf is the only operator I have witnessed who puts on a second glove and examines the cervix at the time of section. If one does not pack the uterus, routinely, this is an excellent procedure.

SUMMARY AND CONCLUSIONS

A review has been made of the 27 hysterectomies associated with pregnancy, labor, and the puerperium at the Coleman Hospital during the time interval embracing 12,536 deliveries. This operation may be the most conservative obstetric operation in certain situations. In this series there was no maternal mortality. Early diagnosis, hysterectomy and radiation is our hope of lowering mortality from chorionepithelioma. In many cases, hysterectomy is preferable to hysterotomy for interruption of pregnancy and sterilization. In degenerated fibroids and fibroids blocking the birth canal, cesarean section at term followed by hysterectomy is the safest procedure, myomectomy being reserved for pedunculated, or easily accessible subserous fibroids. In complete rupture of the uterus early hysterectomy and transfusions are life saving. Severe abruptio placentae occasionally demands section plus hysterectomy but not until conservative management has failed. Placenta accreta when present to any extent, is an indication for hysterectomy. The author considers cesarean section plus hysterectomy the safest abdominal procedure in the infected candidate for cesarean. Thorough intrauterine examination is advocated at the time of cesarean section for evidence of submucous fibroid, abnormal placental implantation or unsuspected injury to the uterus.

REFERENCES

1. Schumann, Edw. A., and Voegelin, Adrian W.: *AM. J. OBST. & GYNEC.* **33**: 473, 1937.
2. Danforth, W. D.: *AM. J. OBST. & GYNEC.* **34**: 365, 1937.
3. Campbell, Ralph E.: *AM. J. OBST. & GYNEC.* **26**: 1, 1933.
4. Huber, Carl P., and Hesselstine, H. Close: *Surg., Gynec. & Obst.* **68**: 699, 1939.
5. De Normandie, Robert L.: *AM. J. OBST. & GYNEC.* **31**: 325, 1936.
6. Irving, Frederick C.: *AM. J. OBST. & GYNEC.* **40**: 621, 1940.
7. Waters, Edward G.: *AM. J. OBST. & GYNEC.* **39**: 423, 1940.
8. Gustafson, Gerald W.: *Surg., Gynec. & Obst.* **64**: 1035, 1937.

DISCUSSION

DR. LOUIS E. PHANEUF, BOSTON, MASS.—In recent years there has been a tendency to decrease the number of hysterectomies following cesarean section, because of the improvement of the technique of the extraperitoneal operation. From the standpoint of infection, many obstetricians feel that they will accomplish as much with the Waters' type of extraperitoneal cesarean section as they would with hysterectomy.

There are cases, however, as shown by Dr. Gustafson, where the existence of a fibroid or of a placenta accreta make hysterectomy necessary. Dr. Gustafson's results following the removal of the uterus after cesarean section have been very satisfactory as shown from his figures. Personally, I have done between 30 and 40 Porro cesarean sections with gratifying results. The convalescence usually is simpler than when the uterus is retained because the process of involution is eliminated.

While I agree that extraperitoneal cesarean section will be responsible for the decrease of radical operations in the presence of sepsis, I feel that the indications brought out by Dr. Gustafson will stand, and that there will always be a place for cesarean-hysterectomy in the practice of obstetrics.

A STUDY OF 104 CASES OF UTERINE FIBROIDS ASSOCIATED WITH ARTERIAL HYPERTENSION*

W. O. JOHNSON, M.D., F.A.C.S., LOUISVILLE, KY.

(From the Department of Gynecology, University of Louisville Medical School)

BE NOT the first by whom the new are tried, nor yet the last to lay the old aside." Can our predecessors admonish us, for today medical literature is filled with the new, but have we learned all we can about the old?

Previously, arterial hypertension has been shown to occur in at least forty-seven syndromes, and grouped under the headings of (1) neurogenic, (2) endocrine, (3) cardiovascular, (4) renal, and in a larger heterogeneous group (5) essential or malignant hypertension.

The works of Goldblatt,⁵ Harrison,⁶ Blalock,⁷ and Page⁴ on experimental renal hypertension and the isolation of renin, renin activator and angiotonin and their effects upon hypertension suffice as an example of the new work on hypertension. Discussions of uterine fibroids and

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

arterial hypertension have been periodic in the medical literature since 1885, and yet the questions are far from settled. The association presents a far more complex problem than hypertension alone.

I wish to present a study of 104 cases of uterine fibroids with arterial hypertension in the hope that further study of this subject may be stimulated.

A criterion for the selection for this series began two years after a hysterectomy for uterine fibroids. All cases reviewed had an admission blood pressure of 165/85 or higher. This series was closely followed in an endeavor to ascertain whether the risk taken in these severely handicapped cases was justified and their salvage was satisfactory.

It has been stated no man should judge the results of his surgical handiwork in the female pelvis unless two summers have passed.

The majority of these patients were on relief or completely incapacitated because of discomfort produced by the fibroids, or the combination of fibroids with myocardial failure. Under the conditions of pain or incapacity one might hesitate to institute surgery when there is little to offer other than relief of pain, and the advisability of taking a great risk may be questioned unless one has a reasonable assurance of the results.

For a period of six years, from 1933 to 1939, there were 708 cases of fibroids admitted to the Louisville City Hospital; 104 of these women were hypertensive; about every seventh patient with fibroids in this series had hypertension. It might be of interest to note that there were 98 colored patients and only 6 white patients, showing the greater predominance of fibroids, a ratio of 16:1, in the colored race. The ratio is usually 9:1. Our youngest patient was 24 years, the oldest 69, both colored (Table I). The average age for both groups was practically the same, 41 years.

TABLE I. AGE AND MARITAL STATUS

RACE	AGE	WEIGHT	MARRIED	DIVORCED	CHILDREN	MISCARRIAGES
White 6	Youngest 36 Average 41 Oldest 54	Lowest 130 pounds Average 157 pounds Highest 185 pounds	2	4	4	Total 3
Colored 98	Youngest 24 Average 40.8 Oldest 69 51 under 40 47 over 40	Lowest 105 pounds Average 156 pounds Highest 235 pounds	8 single 44	46	100 living 36 dead 26% stillbirths	Total 42

A tendency throughout was to obesity, with an average weight of 157 pounds. It has been shown that there is a definite rise in blood pressure increasing with weight for all age groups, and it is three times more frequent in the obese group; obese women are nine times as likely to develop arterial hypertension as those of normal weight. We are thus confronted

with the question, is it the tendency to obesity in such a group which produces the hypertension or the glandular imbalance which has a tendency to develop obesity? The triad of obesity, glandular disturbance and hypertension are frequent findings. Are they causative factors or results?

Fifty-five of the group were 40 years or younger, while 49 of them were over 40 years, the oldest being 69. All but 8 colored women had been married but all had been pregnant, a total of 100 living children, 36 dead; 26 per cent of the deaths were stillbirths. In this group there were 45 miscarriages, making a total of 1.6 pregnancies to each case. This is in contradiction to the statement that women with fibroids are infertile, or women who do not become pregnant develop fibroids. General statements are usually incorrect. Women with fibroids may have proportionately as many children as other women but they have had their children earlier in life.

A study of the clinical symptoms (Table II) revealed the predominant cause of incapacitation to be pain, especially lower abdominal pain or pelvic weight, which was exaggerated when the patient was on her feet. This occurred in 60.1 per cent of the patients as the chief complaint.

TABLE II. CLINICAL SYMPTOMS

RACE	CHIEF COMPLAINT	SYMPTOMS	FINDINGS
White 6	Pain 4—66.6%	Discharge 3—50.0%	Cardiovascular 4— 66.6%
	Bleeding 3—50.0%	Weakness 2—33.3%	disease 6—100.0%
	Enlarged ab- 3—50.0%	Dyspnea 2—33.3%	Fibroids 2— 33.3%
	domen	Ankle edema 1—16.6%	Pelvic inflam-
	Tender ab- 3—50.0%	Constipation 4—66.6%	matory dis-
	domen		ease
	Headaches 3—50.0%		Cervicitis 4— 66.6%
			R. V. O. 1— 16.6%
			Ovarian cyst 1— 16.6%
Col- ored 98	Pain 60—60.1%	Discharge 48—48.9%	Cardiovascu- 46— 46.8%
	Bleeding 34—34.6%	Weakness 18—18.2%	lar disease 98—100.0%
	Enlarged ab- 24—24.4%	Dyspnea 26—26.4%	Fibroids 30— 30.6%
	domen	Ankle edema 20—20.4%	Pelvic inflam-
	Tender ab- 9— 9.1%	Constipation 46—46.8%	matory dis-
	domen	Headaches 29—29.6%	ease
	Frequency 27—27.5%		Cervicitis 24— 24.4%
			R. V. O. 18— 18.2%
			Ovarian cyst 3— 3.0%

Vaginal bleeding associated with anemia was the next most distressing symptom and occurred in 34 per cent of the cases. Enlargement and tenderness of the abdomen ranked third in prevalence of symptoms. It is to be noted that the subjective symptoms were more marked in the white than the colored race.

Other symptoms were complaints of weakness, shortness of breath, edema of ankles, etc., associated more with the anemia or cardiac disturbances than with the mechanics of pelvic pathology.

On initial examination 50 patients, or 48 per cent, had a diagnosis of cardiovascular disease, and in some cases there had been eight years of previous medical treatment for a heart condition.

Pelvic inflammatory disease was present in 30 cases of the colored patients. There were relaxed vaginal outlets in 18 of these. This finding is often overlooked in examination, but is of great importance because, while the fibroid may fill the pelvis, it acts as a support. If one removes a fibroid in the presence of relaxed vaginal floor, usually within one year the symptoms of pelvic discomfort are greater than with the previous condition; therefore it is of the greatest importance in these cases to insure a satisfactory pelvic floor after the fibroid has been removed. Our findings are that, in general, 27 per cent of the patients with fibroids have relaxed vaginal outlets which necessitate perineal repair.

Our laboratory findings (Table III) reveal the greatest anemia in the colored cases. It seems incredible that persons could exist with hemoglobin ranging from 24 to 32 per cent as were recorded upon admission; however, the average was 71 per cent by the Sahli method. In some of the inflammatory cases there was a leucocytosis.

TABLE III. LABORATORY FINDINGS

RACE	R.B.C.	W.B.C.	HG. (SAHLI)	WASSER- MANN	URINE	N.P.N.	UREA CLEAR- ANCE
White 6	Lowest	Lowest	Lowest	Positive 1 16.6%	Albumin 2	Lowest	Normal
	3,582,000	3,400	60%			24.0	80-120
	Average	Average	Average			Average	Average
	4,073,000	6,700	70.4%			25.1	100%
Colored 98	Highest	Highest	Highest	Positive 26 37.7%	Albumin Trace 45	Highest	
	4,840,000	10,000	85%			26.0	
	Lowest	Lowest	Lowest			Lowest	Lowest
	1,680,000	2,600	30%			24.0	45%
	Average	Average	Average			Average	Average
	3,910,000	8,180	71.6%			30.1	77%
	Highest	Highest	Highest			Highest	Highest
	5,270,000	32,350	90%			39.6	117%

Evidence of syphilitic infections was present in 16.6 per cent of the white women and in 37.7 per cent of the colored cases. This is slightly higher than the general average of positive serologic reports, which in the Louisville City Hospital was about 3 per cent for white and 23 per cent for colored individuals. This higher incidence of syphilitic infections may have a bearing on the increase of hypertension; we know that vascular changes are frequently the result of syphilitic infections.

About 50 per cent of the patients had a trace of albumin in the urine, and practically no cellular pathology of significance. As far as routine urinary tests are concerned as a single test, or even in a series they are of little value in determining kidney capacity or damage. We find that a carefully carried out Mosenthal test is of some benefit in determining renal damage.

Page⁸ has demonstrated the use of newer renal function tests with diodrast and phenol red, which are used to measure the renal blood flow, and inulin, in measuring the efficiency of tubular tissue. In hypertension he found the renal blood flow is decreased while the glomerular filtration and tubular mass are increased.

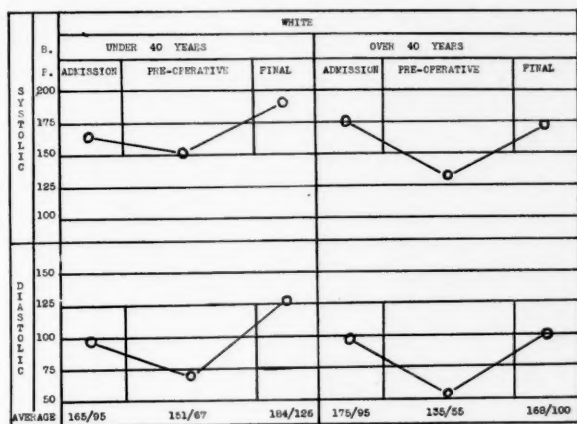


Chart 1.

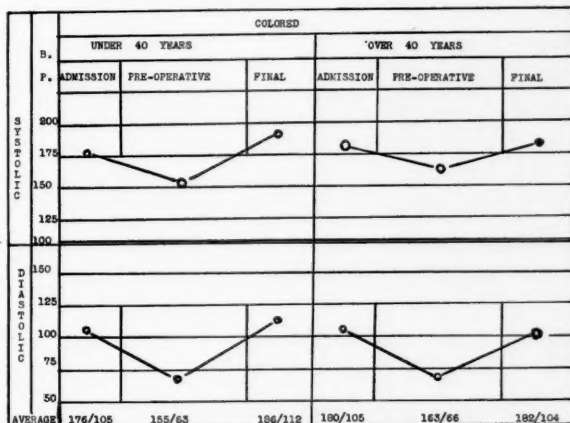


Chart 2.

Yet all of this does not give one the limitations of renal functions, and only a slight indication as to the extent of renal damage. It does not approach a means of estimating the gravity of such cases, the capacity of recuperative power of such damaged kidneys, or the risk involved. Under adverse circumstances one has a tendency to avoid great surgical risk primarily for the relief of pelvic pain, for in these cases one can expect only indirectly to relieve or improve the hypertension and myocardial damage, so we must conclude the risk is taken primarily for the relief of pelvic pain.

A study of the blood pressure over a period of time was informative. In both the white and colored patients the blood pressure levels before the age of 40 years were lower, the white being about 20 points lower than the colored; the greater fall in both systolic and diastolic pressures was noted in the colored with rest and treatment. This was probably due to the general systemic improvement in colored patients. In the final readings, taken from two to six years after operation, both groups under forty show a progressive rise in both systolic and diastolic pressures over that of preoperative findings (Charts 1 and 2).

In only five instances were there falls below the initial admission pressure, and these occurred in the group of patients under 40 years of age. Was this the result of the intervening years of increased activity, or previously impaired cardiovascular systems, or progressive changes in susceptible individuals? It does point out conclusively that, so far as fibroids and hypertension are concerned, nonspecific operations upon pelvic pathology do not permanently lower the blood pressure, nor does it seem to prevent its gradual expected rise in later years. From consideration of blood pressure alone, it seems that fibroids are only an associated finding, or fibroids would be found earlier in life and more frequently associated with hypertension. With proper handling, the risk in such cases is no greater than the average major pelvic operation by age grouping.

In patients over 40, the initial pressure was higher, the improvement from rest was greater in the white than in the colored group, but almost invariably the previous pressure returned or was slightly higher in both groups. This elevation began with activity of the patient and eight years after operation had not changed appreciably. Study of charts on blood pressure changes shows with age an increased incidence of hypertension, e.g., Gager¹ in a series of 500,000 life insurance examinations, reports:

YEARS	SYSTOLIC	DIASTOLIC
20-29	3.9%	3.4%
30-39	11.6%	8.9%
40-49	22.2%	27.0%
50-	36.7%	31.5%

As the average age of our group is 41 years, one would expect a certain percentage of rises in pressure to be associated with age.

Tables IV and V show the menstrual records of these patients. A predominant number of patients had regular periods, and in the colored race flooding was present in over 30 per cent. Colored patients frequently have given a history of bleeding for two years without treatment, have shown a hemoglobin of 35 per cent or less, and have presented no alarm over the condition.

Excessive menorrhoea should not be considered as evidence of a polyglandular state, but as a manifestation of a deficiency which results in a

TABLE IV. MENSTRUAL RECORD, WHITE

DURATION		REGU- LAR	IRREG- ULAR	MENO- PAUSE	FLOOD- ING	DIS- CHARGE	CLOTS	PAIN
Under 40 years	2	4	0	0	0	2	1	2
	4-5 days							
	2 5-7 days							
Over 40 years	1	2	0	0	1	0	1	2
	3-4 days							
	1 7-8 days							

TABLE V. MENSTRUAL RECORD, COLORED

DURATION		REGU- LAR	IRREG- ULAR	MENO- PAUSE	FLOOD- ING	CHARGE DIS-	CLOTS	PAIN
Under 40 years	75% 3-5 days	40	3	2	12	28	20	18
	17% 6 days							
	8% 10 days							
Over 40 years	12 none	35	6	12	16	32	23	21
	86% 3-5 days							
	2% over 6 days							

premature disintegration of the corpus luteum and consequently a hastening in the appearance of menstruation. This is substantiated in cases of fibroids where the growths produce mechanical and circulatory deficiencies of the endometrium and are associated with cystic follicular degeneration of the ovaries and fibrosis and early degenerative changes in corpora lutea. The commonest cause of profuse menses is due to some kind of interference with the mechanism which controls the flow of blood to the desquamating endometrium. Fibroids play a large part in the distortion of musculature, and disturb by congesting the pelvis and affecting ovarian secretion.

In 14 of the colored women, the menopause had taken place from six months to twelve years earlier. Previously these patients sought relief from incapacitation, caused by pelvic pain in most instances. The belief has long been held that once the menopause has begun fibroids will reduce and cause no further trouble. Frequently fibroids cause more pain after the menopause because of disturbances with adhesions than was complained of during active menstrual life; also, one should keep in mind the fact of malignant degeneration in growths after the menopause.

In this series, one white and 34 colored patients, or 33.6 per cent, had complete hysterectomy (Table VI); 5 white and 64 colored patients, or 66.3 per cent, had supravaginal hysterectomy with practically the same mortality (1.8 per cent); 37 had hysterectomy and salpingectomy without removal of ovaries. When possible, the tubes were left in place for better blood supply to the ovaries. Fifty-two had incidental appendectomy. Unless the appendix was definitely involved in old adhesions or there was evidence of pathology, it was deemed wise not to disturb it because of increase in the risk. It was not the time element in removal

TABLE VI. OPERATIONS

RACE	TYPE		TIME OF OPERATION	TYPE ANESTHESIA	IMMEDIATE RESULTS
White 6	Complete hysterectomy 1 Supravaginal hysterectomy 5	Bilateral salpingectomy 4 Bilateral oophorectomy 3 Appendectomy 4 Perineorrhaphy later 2	Shortest 1 hr. 15 min. Average 1 hr. 33 min. Longest 1 hr. 55 min.	Spinal 6	Improved 6
Colored 98	Complete hysterectomy 34 Supravaginal hysterectomy 64	Bilateral salpingectomy 25 Bilateral oophorectomy 33 Unilateral ooph. 26 Appendectomy 48 Perineorrhaphy 17	Shortest 35 min. Average 1 hr. 48 min. Longest 3 hr. 8 min.	Spinal 68 Local 3 Gas oxygen 2 Cyclopropane ether 21 Ether 4	Improved 94 Died 4

of an incidental appendix, but the additional disturbance of another system which might prove too heavy a load for a bad risk patient.

Perineorrhaphies were done in 19 patients. We felt that this was important in this particular group of cases, and the procedure was usually carried out after the major operative work had been completed without prolongation of anesthesia.

Regardless of common belief, time consumed at operation is an important element in these cases and our set-up with the Louisville City Hospital is such that severe cases are the ones operated upon by the visiting staff and the time element, never to the detriment of accuracy, is one to be observed. The average time for all cases was one hour and forty minutes; in some of the more critical cases only thirty-five minutes was necessary for a complete hysterectomy.

The type of anesthesia is an important factor. At first these patients were conditioned for an average period of ten days, and low spinal anesthetics were given. Seventy-four of the 104 cases were done under spinal anesthesia under the supervision of the Department of Anesthesia.

Deaths were as follows:

- 1, spinal anesthesia, pulmonary edema (two weeks postoperative, second closure).
- 1, spinal anesthesia, bronchopneumonia, three days postoperative.
- 1, local anesthesia, nephritis and uremia, ten days after.
- 1, cyclopropane anesthesia, cerebral hemorrhage, and cardiovascular disease.

The disturbing factors were, in spite of carefully prepared patients and low spinals with small dosages, that these cases with hypertension

would have a marked drop in blood pressure which could not be controlled by synephrine or adrenalin, or coramine, and in some cases would have a very slow return of pressure to normal. This was followed usually by a disturbance in urinary output, which is to say the least quite disturbing for a few days, but with forced glucose intravenously, and other supportive therapy the kidney function gradually returned to the previous levels. For these reasons we have been trying to adapt the anesthesia to the patient, rather than the patient to the anesthesia, and have used more inhalation anesthesia of late which can be more completely controlled. This has not been entirely satisfactory, for in these large growths relaxation is important for exposure and removal of the tumor. Our present regime is a combination of cyclopropane with ether only for a short period of relaxation in the deep phase of the anesthesia.

TABLE VII

HOSPITAL DAYS				POSTOPERATIVE COMPLICATIONS	
	WHITE		COLORED		COLORED
	Lowest	21 days	Lowest	16 days	
Under 40 years	Average	24 days	Average	24 days	2 Wound infections and transfusion
	Highest	28 days	Highest	50 days	1 Shock and transfusion
					1 Infected wound, secondary closure
Over 40 years	Lowest	21 days	Lowest	9 days	2 Shock and transfusion
	Average	24 days	Average	23 days	2 Wound infections
	Highest	27 days	Highest	59 days	1 Pyelitis
					1 Bronchopneumonia
					2 Upper respiratory infections (mild)
					1 Cardiac failure, responded to digitalis
					1 Wound infection, strep. peritonitis, pulmonary edema
					1 Toxic nephritis and uremia
					1 Metastasis papillary adenocarcinoma

With an average preoperative preparation of ten days (Table VII), these patients had average hospitalization of only twenty-four days, and a surprisingly smooth convalescence, the lowest 16 days, and the longest 73 days. Major complications included: 6 wound infections with 2 necessitating secondary wound closure, 3 cases treated for shock, 1 death from bronchopneumonia, 2 other slight upper respiratory infections, 1 acute cardiac failure which responded to digitalis therapy, and 1 uremia. Seventy-five per cent of the complications appeared in the over 40-year-old colored group and the convalescence in this group was slower.

A study of the pathology reports is illuminating. All patients had multiple fibroids; they were studied only to rule out malignancy, which was found in only one patient (microscopically), and was not considered clinically important. That patient is living and well four years postoperatively.

Our cases were grouped clinically as to phase of menstrual cycle patient was in at time of operation, by ascertaining the cycle, and then taking the date of last menstrual period and estimating what phase the endometrium should be in, grouping into:

1. Premenstrual
2. Menstrual; or those bleeding at time of operation, or calculated to be at menstrual period
3. Postmenstrual
4. Menopause

With this clinical grouping we studied only the cases which had ovarian and endometrial pathologic findings (Tables VIII, IX, and X). Our conservatism makes our material small for this group. Thirty-seven patients did not have the ovaries removed. We believe this conservatism was of great advantage to the patient even if a loss to science.

We believe that the monthly proliferative changes in the endometrium are based on follicle activity, and that secretory and premenstrual changes are due to the corpus luteum activity. The amount of hormone

TABLE VIII. WHITE

CLINICAL PHASE		AGE	ENDOMETRIAL PATH. REPORT	OVARIAN PATH. REPORT
Under 40 years	Premenstrual 2	37 yr.	1 Premenstrual endometrium secretory 1 Atrophic endometrium Chronic endometritis	1 Retention follicle cyst Corpora albicantia 1 Retention follicle cysts Fibrosis
Over 40 years	Menstrual 1 Postmenstrual 1	48 yr.	1 Polypoid hyperplasia 1 Polypoid hyperplasia	1 Fibrosed with follicle cysts 1 Fibrosed with follicle cysts

TABLE IX. COLORED PATIENTS, UNDER 40 YEARS

CLINICAL PHASE	AGE YR.	ENDOMETRIAL PATH. REPORT	OVARIAN PATH. REPORT
Premenstrual 6	35.4	3 Hyperplastic endometritis 2 Early interval endometrium (nonsecretory) 1 Chronic atrophic endometritis	3 Retention cysts with corpus luteum cysts and fibrosis 1 Papillary cystadenoma (benign) 1 Corpus luteum cyst 1 Atrophic ovary
Menstrual 5	35	5 Chronic hyperplastic endometritis	1 Granulosa cell tumor 3 Retention follicle cysts 1 Fibrosed ovary
Postmenstrual 12	35	9 Hyperplastic polypoid endometrium with lymph. infiltration 3 Late interval endometrium	6 Retention follicle cysts with corpus luteum 3 Retention follicle cysts 2 Fibrosed ovaries 1 Ovarian abscess
Menopause 4 6 mo.-2 yr.	36	2 Hyperplastic endometritis 1 Atrophic endometrium 1 Premenstrual endometrium	2 Fibrosed ovaries with retention follicle cysts and corpus luteum cysts 1 Fibrosed ovary, no cysts 1 Retention follicle cysts

will determine, in a sense, the amount of reaction (or secretion) shown in the endometrium; increased follicular activity will lead to increased growth of endometrium.

TABLE X. COLORED PATIENTS, OVER 40 YEARS

CLINICAL PHASES	AGE YR.	ENDOMETRIAL PATH. REPORTS	OVARIAN PATH. REPORTS
Premenstrual 12	43.5	4 Fibrosed endometrium 7 Polypoid hyperplastic endometrium 1 Premenstrual (nonsecretory)	11 Retention follicle cysts with fibrosis of ovary 1 Retention follicle cyst and corpus luteum
Menstrual 5	44.5	3 Chronic endometritis 1 Atrophic endometritis 1 Early menstrual (secretory)	1 Papillary cystadenoma 1 Bilateral dermoid cyst 2 Retention follicular cyst 1 Retention follicle cyst, degenerated luteum cyst
Postmenstrual 10	46	5 Atrophic endometritis 4 Polypoid hyperplastic endometrium 1 Late interval endometrium	5 Retention follicle cysts with fibrosis 4 Retention follicle cysts with corpus luteum 1 Retention follicle cyst
Menopause 8 6 mo.-12 yr.	52.7	4 Polypoid hyperplastic endometrium 3 Atrophic endometritis 1 Adenocarcinoma (fundus)	6 Retention follicle cysts with fibrosis 1 Calcified dermoid ovary 1 Adenocarcinoma metastasis

Analysis of the findings, as is shown in Tables VIII, IX, and X, permits the following conclusions: (1) A woman can bleed from any type of endometrium. (2) Polypoid hyperplasia of endometrium is seen with retention follicular cysts of the ovaries, with or without luteal cysts. The predominant finding is that 64 per cent of fibroids have corpus luteum cysts. (3) Chronic endometritis with retention cysts of ovaries is evidence of old pelvic infections. (4) Atrophic endometritis with follicle retention cysts and ovarian fibrosis are seldom associated with corpus luteum cysts. (5) The unusual findings in this small, unselected group were dermoids, papillary cystadenoma and granulosa cell tumor and carcinoma of fundus.

In 14 of the cases which were from six months to twelve years postmenstrual, as decided by cessation of bleeding and not by age, the fibroid growths continued with symptoms which incapacitated the individual. Persistent symptoms with abdominal growths after the menopause suggest possible malignant changes and we believe warrant surgery.

In 3, or 21.4 per cent, of these postmenopausal cases, secretory changes were found in the endometrium. It has definitely been proved that follicle growth and even ovulation with corpus luteum formation occurs months or even years after the menopause. This fact should make us more conservative about oophorectomies.

Endometrial studies indicate that ovarian activity may revive spontaneously and lead to periods of bleeding. Such a finding should not

lessen our vigilance for carcinoma. Briepohl,³ in 130 cases of post-menstrual bleeding, found a stage of proliferation in 10 per cent and a secretory phase in 2.3 per cent, a hyperplasia of the endometrium in 11.5 per cent, all of which indicate a stimulation of the endometrium by ovarian hormones after menopause. This demonstrates that the ovaries may be re-activated and that the endometrium itself may respond after it has become atrophic, and that both have functional possibilities after the menopause and should not be promiscuously removed.

TABLE XI. CAUSES OF DEATHS

UNDER 40 YEARS		OVER 40 YEARS	
<i>Hospital Deaths</i>		<i>Hospital Deaths</i>	
1 Nephritis and uremia		1 Bronchopneumonia	
		1 Nephritic toxemia	
		1 Pulmonary edema (2 wk. secondary closure)	
<i>Under One Year</i>		<i>Under One Year</i>	
1 Heart failure		1 Cardiovascular disease	
<i>Under Two Years</i>		1 Myocarditis	
1 Cardiovascular disease		1 Heart failure	
		1 Lobar pneumonia	
		1 Cancer fundus uteri	
<i>Two to Six Years</i>		<i>Two to Six Years</i>	
1 Cardiovascular disease		1 Heart failure	
1 Pulmonary tuberculosis		1 Stroke	
1 Stab wound shoulder, pneumonia		1 Cerebral hemorrhage	
1 (White) Cardiovascular disease		1 Fracture of vertebra, cord lesion	
		1 Carcinoma cervix	

Causes of deaths are given in Table XI. Salvage of the group is shown in Table XII, with hospital death rate of 3.8 per cent and a total eight-year mortality of 19.2 per cent. We feel that we have restored a debilitated, greatly handicapped group to greater capacity.

TABLE XII

	WHITE			COLORED					
	LIVING AND WELL	RELIEF	DEATHS UNDER 2 YR.	LIVING AND WELL	RELIEF	HOSP. DEATHS	DEATHS UNDER 2 YR.	DEATHS 2-6 YR.	TOTAL MOR-TALITY
Under 40 years	2	2	1 H.C. V.D.	25	13	1 1.02%	2 2.04%	4 4.08%	7.6%
Over 40 years	1	1	0	35	6	3 3.06% Total 3.8%	4 4.08%	5 5.1%	11.5% Total 19.2%

Let us look into the rehabilitation of this group (Table XII). In the white patients we have one dead, 50 per cent working and 50 per cent on relief but comfortable, and able to be about better than before. In the colored we have 65 working and apparently well for years, 19 on relief and definitely subjectively relieved. Some are incapacitated by progression of heart condition. Only 3 of these may be classified as hopeless at present.

Many of these cases have been seen from time to time in the clinical follow-up over years. In the final follow-up of these cases, all are accounted for. Four were heard from in other states and not directly checked. There were 5 special clinics held in which 65 per cent of the patients were seen. The deaths and their causes were checked through the Bureau of Vital Statistics of Kentucky State Board of Health, and those living and on relief were checked through the Municipal Bureau and Family Service Organizations, and some of those unable to come in for observation were contacted in their homes. This phase of the study alone was very exhaustive, but most instructive.

SUMMARY

1. Presentation of 104 cases of uterine fibroids with hypertension, which were studied from two to eight years after operation.
2. Presentation of effects of rest on blood pressure, and showing that it is not materially affected by operation, nor does operation prevent its later rise.
3. Comparative study of symptoms, findings before and after forty years of age with deductions.
4. Detailed study of endometrium and ovaries in cases where removed in relation to clinical cycle of menstruation and discussion, showing that in 21 per cent of cases after menopause there is evidence of continued ovarian function.
5. Causes of deaths given at different periods after operation.
6. Mortality and salvage in this series show that these cases when handled properly do not have greater mortality than the average major pelvic operations for age grouping, with satisfactory salvage.

REFERENCES

1. Gager, Leslie T.: Hypertension, Baltimore, 1930, Williams & Wilkins Co., p. 49.
2. Fetter, F., and Schnabel, T. G.: Arch. Int. Med. 55: 609, 1935.
3. Briepohl, W.: Zentralbl. f. Gynäk. 59: 1998, 1935.
4. Page, I. H.: Proc. Soc. Exper. Biol. & Med. 35: 112, 1936.
5. Goldblatt, H.: Ann. Int. Med. 11: 69, 1937.
6. Harrison, R. R., Blalock, A., Mason, M. F., and Williams, J. R., Jr.: Arch. Int. Med. 60: 1058, 1937.
7. Blalock, A., Levy, S. E., and Cressman, R. D.: J. Exper. Med. 79: 833, 1939.
8. Page, I. H., and Helmer, O. M.: Central Soc. Clin. Res. 12: 17, 1939.

908 BROWN BUILDING

DISCUSSION

DR. PAUL TITUS, PITTSBURGH, PA.—An important point perhaps was lost in the figures: Dr. Johnson's emphasis that perineal repair should be done when indicated in addition to the operation for fibromyomas. Out of this large group of fibroids, 13 per cent showed hypertension. Does this mean that fibromyomas tend to cause hypertension? I think Dr. Johnson wants to indicate to us that it should not be given such interpretation. He said that blood pressure and cardiorenal conditions are not disturbed, favorably or otherwise, by fibromyomas. I should like him to clarify that point.

Did I understand Dr. Johnson to state that hypertension complicating fibromyomas as an added risk may be discounted? It seemed to me that the mortality rate of the patients with hypertension was higher than that of the average group of patients undergoing operation.

DR. WILLIAM T. MCCONNELL, LOUISVILLE, KY.—Dr. Johnson and I have worked together for many years, and I am familiar with this particular series of cases. This does not represent a cross section of cases dealing with fibromas per se. This series he has reported is a study of the possibilities of salvage of the old "crocks." There is no intelligence in their seeking health but they come because they are in pain, and they are in a very bad physical condition. It takes skill and courage to tackle these cases. This report covers the possibility of rehabilitation of a class of patients who are a burden to society and a misery to themselves. The paper shows to me what can be done in the matter of relieving suffering and a certain amount of economic strain on the body politic.

DR. F. S. WETHERELL, SYRACUSE, N. Y.—I would like to have Dr. Johnson clarify the matter of hypertension in relation to hysterectomy for fibroids.

DR. JAMES E. KING, BUFFALO, N. Y.—The mortality of hysterectomy in itself is not to be feared today, because we have repeated instances of reports of cases, 300, 400, 500, 600, without a death. In my own series I have had 530 consecutive hysterectomies without a death. In that number, of course, were a considerable number of hypertensive cases. In my own work I have drawn an arbitrary line which indicates when I am dealing with a case which is possibly going to give trouble. Any woman who has a blood pressure of 170 or above I regard with considerable anxiety.

A few years ago I analyzed 537 patients upon whom I had performed a hysterectomy, and of that number 65.7 per cent had a blood pressure of 120 to 170 systolic. These do not worry me. But 8.6 per cent of the 537 patients had a blood pressure of 170 to 220. Now that 8.6 per cent did worry me. With a more careful selection of the anesthesia, we are not in the same position that we were a few years ago when ether was generally used.

I would like to know whether Dr. Johnson has any particular line of procedure in preparing his patients for hysterectomies? I think his mortality was a little high for the present day, but I presume the average Negroess is not altogether a very suitable person for any type of abdominal surgery.

DR. WILLARD R. COOKE, GALVESTON, TEXAS.—Dr. Johnson is dealing with a type of fibromyoma and a type of patient with which we are all familiar in the South. Neither the patients nor the fibromyomas are like those encountered among the general population of New York or Pennsylvania. For the type of case with which Dr. Johnson is dealing, his mortality is definitely low, for I know that in many hospitals the mortality in such cases has run from 6 to 10 per cent.

I once spent ten years in studying the blood pressures in such cases before and after operation and concluded that hypertension was not essentially a very serious factor of this type of operation.

DR. WALTER T. DANNREUTHER, NEW YORK, N. Y.—After a modest experience with hysterectomy extending over a good many years, I have come to the conclusion that hypertension per se is of little consequence. The essential factors are the associated obesity, renal damage, compromised myocardium, or impaired metabolism.

The important therapeutic items, which can be carried out with derelicts as well as with other women, are careful preoperative study and preparation of all patients.

I also believe that cyclopropane anesthesia, given by an expert, and an expeditious operator are additional important factors of safety, in patients who are relatively poor risks.

DR. JOHNSON (closing).—My purpose in this paper was to present the findings in a group of cases and analyze the results to see whether the surgical risk, money expended by the hospital, and salvage of cases justified continuation of this work. These patients were relief cases from the Work House, Poor People's Home, and Home of the Invalids. The procedure was carried out with the hope of offering them relief from discomfort and for possible rehabilitation.

In these cases, we operated principally for pelvic pain, and no attempt was made to consider or prove the relationship between the fibroids and hypertension. This association was mentioned because it is frequently found in such bad risk cases. I tried to point out, however, that nonspecific operations on the pelvis had no effect upon lowering of the blood pressure, and apparently do not prevent its subsequent rise in later years.

All patients were carefully prepared from a medical viewpoint, with rest, diet, digitalis and other measures as indicated, for an average of ten days before operation. The determination as to the optimum time for operation requires the greatest consideration and care.

Dr. Titus has stated that 10 per cent of cases of fibroids have hypertension. I did not wish to infer that a certain percentage of fibroids had hypertension, but simply wished to state that about one case in every seven admissions of fibroids had hypertension, and that 18 cases of our series had relaxed vaginal outlets which, we feel, it is important to repair in association with or following hysterectomy.

In these cases, mortality records cannot be considered, but from an analysis of this series over a period of eight years, we feel it is worth while operating upon them for the relief of pain, that the mortality rate is not prohibitive, that the salvage is satisfactory, and renders an apparently hopeless invalid who is on relief, comfort and at least a 60 per cent chance of earning a livelihood.

PATHOLOGY OF THE EMBRYO AND ABORTION

A. K. PAINE, M.D., BOSTON, MASS.

(From the Departments of Obstetrics and Pathology, Tufts College Medical School)

THE accumulating results of studies of spontaneously aborted products of conception seem to necessitate a revision of our approach to the clinical problems involved.

It is conceded that at least 10 per cent of all pregnancies end in spontaneous abortion.^{1, 2} Of these something approaching 90 per cent disclose pathology of the conceptus absolutely or relatively incompatible with a continuing pregnancy.³ In the former early death of the embryo results; in the latter the embryo in spite of pathology may continue to grow with resultant gross fetal defects, monsters, hydrocephalus, spina bifida, etc., a potential 12 per cent according to Mall.⁴

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

The etiology may be intrinsic in the sense of male or female germ plasm defects or in defective cell union. The trophoblast may fail to establish itself normally, due to endometrial faults, histologic or functional, any of which may prevent or interfere with a subsequent development of the embryo proper. If death of the embryo occurs early, an atypical growth of the chorion may continue as a cystic degeneration.

Storch⁵ reported this in 1878 and estimated its incidence as 75 per cent. Hertig³ found it in 66.9 per cent of the material he has studied and suggests that this early cystic degeneration is a potential first phase of the true mole the invasive type of which in turn, as Phaneuf⁶ has described, is the genesis of chorionepithelioma.

Early cystic degeneration is so common, a true mole so rare, the correctness of Hertig's contention seems questionable. If it were correct, the early expulsion of this defective ovum would appear as an important defense mechanism.

When an abortion actually occurs, post facto findings indicate we were most frequently dealing with the terminal phase of an inevitable process, the end result of an already interrupted pregnancy. In no correct sense can any part of the clinical picture be designated as a threatened abortion. Streeter⁷ has further emphasized the important fact that death of the embryo usually precedes by several weeks, its eventual expulsion.

Besides this early pathology, there are encountered various disorders (anatomic anomalies and malpositions) of the placenta. Hertig³ in his series found a 9 per cent low implantation, confirming our clinical suspicion that a definite number of abortions are in reality early placenta previas.

In the abortion which has this definite background of pathology, attempts to prevent expulsion would obviously be ill advised, perhaps unsafe, eventually futile. Its urgent clinical problems are in its complications: incompleteness, hemorrhage, and sepsis.

The clinician's difficulties, however, are not limited to these cases *with the definite pathology* which abort, for he encounters a considerable group of patients having symptoms indicating the possibility of abortion but in which it may or may not occur. If it does occur, the percentage probabilities indicate pathology of the conceptus, but it may belong to that 10 per cent which histologically shows only the usual hemorrhage, evidences of infection, inflammation and necrotic changes. One's impression is that these cases are quite numerous but a tabulation of 500 consecutive cases delivered at term in the Booth Hospital disclosed only a 3.8 per cent incidence of early pregnancy staining or bleeding.

What happens in the patient not aborting is conjectural. A partial disturbance of placental attachment may be a reasonable hypothesis.

Some intercurrent interference with an otherwise normal pregnancy with a further deduction that a not too extensive primary process may permit regeneration and repair. To delay expulsion until this process of repair can establish itself is most important.

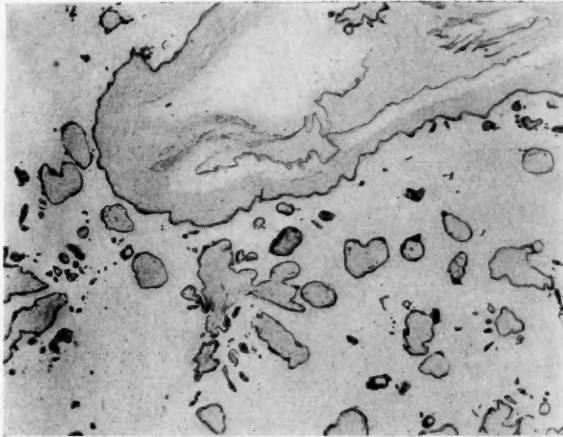


Fig. 1.—Cystic degeneration of the chorion from a defective ovum, forty-six days after the onset of pregnancy, showing a portion of the wall of the chorionic sac, with scattered villi lying near by. The chorionic sac is bordered externally by a narrow uninterrupted syncytium which lies on a layer, varying in thickness, of loose connective tissue showing here and there large and smaller poorly delimited cystlike accumulations of fluid. There are few lacunae-like endothelial-lined spaces containing the remnants of disintegrating nucleated red blood cells. This chorionic sac is lined internally by a somewhat smaller thin-walled sac lined by flattened out squamous-like cells. This latter layer of cells formed the inner wall of the whole sac. The villi are comparatively few in number and unusually simple in design. They are coarse, bulky, and show little tendency toward branching. The stroma is both absolutely and relatively increased in proportion to the bordering trophoblastic layer. (X14.)

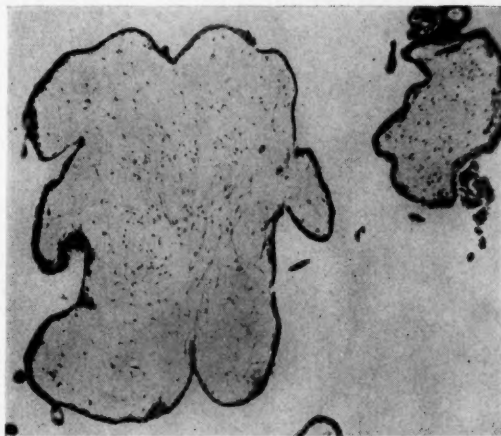


Fig. 2.—A higher power of one of the villi shown in Fig. 1, simple in design, poorly differentiated, lacks well-developed branching processes, and instead shows only few protruding buds. The stroma is distended and edematous, showing clear spaces filled with fluid. The intercellular fluid lacks any tinctorial reactions. The stroma is composed of spindle and spiderlike cells whose processes join one another. In this, no vessels are clearly demonstrable, and in this villus there are no developing red blood cells. The edematous stroma is bordered by a thin and inconspicuous trophoblastic wall. Only at two points is there a slight tendency toward syncytial budding. (X76.)

In the light of present knowledge it seems then that we have two major premises.

First: The clinical picture of an abortion may, and most commonly does, represent the expulsion of a defective (already dead) ovum. Any



Fig. 3.

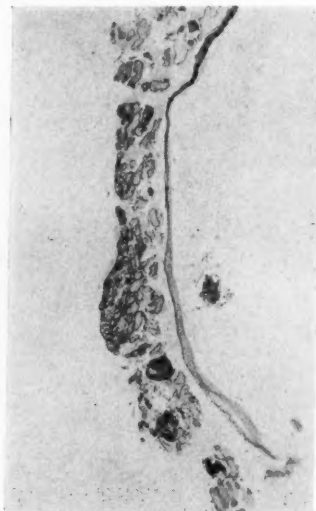


Fig. 4.

Fig. 3.—A still higher magnification of portion of villus seen in Fig. 1, showing the limiting trophoblastic wall, and its sharp separation from the underlying edematous stroma. Here the syncytium and Langhan's layer of cells may be clearly separated. The syncytium is orderly. There is a well-developed brush-border, the relative ratio of nuclei to cytoplasm favors the latter. The nuclei are uniform in size, shape, and staining; in places they are clumped. The Langhan's layer forms a continuous and monotonously uniform line of cells beneath the syncytium. These cells have pyknotic nuclei, their cytoplasm is clear and vacuolated. No mitoses are seen. The picture is one of hypoplasia. ($\times 600$.)

Fig. 4.—Defective embryo, 8 weeks, sac discharged intact, showing a sac bordered by a rather sparse zone of chorionic villi. Within the sac is only a single small nest of cells. This was loosely adherent to the inner surface of the cyst by a delicate transparent threadlike stalk. ($\times 6$.)

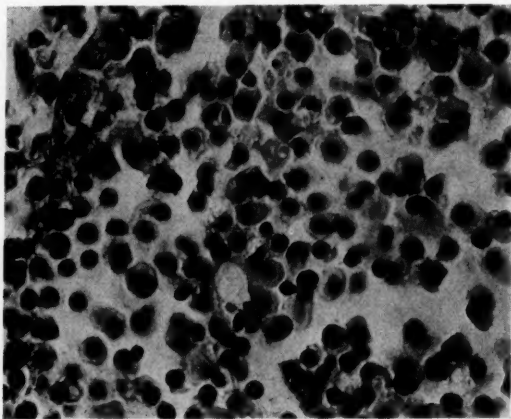


Fig. 5.—A high-power magnification of the small nodule found within the cyst, shown in Fig. 4. This small nest is almost entirely composed of developing red blood cells that lie within distended lacunar spaces. This island of erythropoietic tissue was the only remnant of embryonic tissue present. ($\times 640$.)

attempt to prevent its expulsion, if not actually harmful, serves no useful purpose.

Second: There may be an intercurrent disturbance of an otherwise normal pregnancy, a true threatened abortion, exact opposite of the first mentioned premise, in that every effort to prevent expulsion is required.

From this derives an urgent clinical need, the ability to determine in advance of the eventuality with which group we deal in a given case. If practice would keep step with scientific progress to avoid treatment absurdities, it must set up clinical criteria for this differential diagnosis. Toward this end we have something of a start. For instance, on a percentage basis most of the irreparable pathology will be encountered in the early abortions. Excessive and prolonged bleeding is significant. Temperature elevation is almost pathognomonic of a terminated pregnancy.

The treatment of abortion is not germane to the subject of this communication but certain of its aspects are pertinent. The testimony of a voluminous and enthusiastic literature as well as common observation indicates that present-day therapy centers largely in the use of corpus luteum hormone and in the administration of vitamin E though candor may compel us to admit that much of it seems hardly more than testimonial evidence.

Concerning vitamin E, advocated originally for habitual abortion,⁸ it is now very generally employed in the treatment of any abortion. There are probably few patients today beginning to bleed during early pregnancy, who do not get wheat germ oil. Without consuming any time analyzing the reasoning involved, it might suffice to say that if vitamin E deficiency plays much part in the cause of abortion, we would have had considerable opportunity in clinical observation to realize that fact. I refer to the severe nausea and vomiting cases. Here there is of necessity a marked deficiency in vitamin E intake, along with everything else, and yet about the only thing these patients *never do* is to abort spontaneously.

The common reason for the employment of hormones is as substitution therapy. It is very obvious that a progesterone deficiency may play a background part in some pathology of the ovum,⁹ the abnormal endometrium, faulty nidation, failure of the trophoblast sequence, but if so, it represents a fait accompli, long before the clinician begins to deal with the abortion.

A function, more correctly perhaps, an attribute of progesterone, has been described by Falls¹⁰ and others, whose experiments indicate its inhibiting effect on uterine contractions. This would seem the rationale of its use in threatened abortion but, and important, a *very definite contraindication* for its use in the woman expelling a pathologic ovum. On the other hand, Kurzrok¹¹ reports increased uterine contractibility

following its administration, and Hamblen¹² has recently introduced another disconcerting note, suggesting that large doses of progesterone, by interfering with intrinsic progestin metabolism may precipitate abortion. He further suggests that its administration may also interfere with therapy in thyroid dysfunction, the importance of the latter already having been emphasized by Litzenberg,¹³ Bloss,¹⁴ and many others.

It would seem, from the conflicting evidence, that the value of the corpus luteum hormone in the treatment of abortion is still an open question.

CONCLUSIONS

In the light of present knowledge, the clinician is justified in concluding:

1. That most spontaneous abortions occur as a result of pathology of the conceptus incompatible with continuing pregnancy and that the clinical picture of abortion here represents in reality a terminal phase of an already interrupted pregnancy.
2. That a smaller group is encountered in which some intercurrent "accidental" type of pathology develops in an otherwise normal pregnancy, in which abortion may or may not result, and to which the clinical term "threatened abortion" correctly applies.
3. That intelligent management of abortion requires first a differential diagnosis, determination in advance to which group a given case belongs.
4. That in the treatment of "threatened abortion" there should be no question of the safety of any therapy employed and at least, a reasonably understandable justification for its use.

REFERENCES

1. Taussig, E. J.: Abortion, St. Louis, 1936, The C. V. Mosby Co.
2. Malins: J. Obst. & Gynaec. Brit. Emp. 3: 307, 1903.
3. Hertig, A. T., and Edmonds, E. W.: Arch. Path. 30: 260, 1940.
4. Hall, F. P.: Am. J. Anat. 22: 49, 1917.
5. Storch, E. D.: Virchows Arch.-Path. Anat. 72: 582, 1878.
6. Phaneuf, L. E.: New England J. Med. 217: 770, 1937.
7. Streeter, G. L.: Contributions to Embryology, Carnegie Inst. of Washington, No. 55, p. 28.
8. Vogt-Møller, P.: Acta obst. et gynec. Scandinav. 13: 219, 1933.
9. Pratt, J. P.: Endocrinology 11: 195, 1927.
10. Falls, F. H., et al.: J. A. M. A. 106: 271, 1936.
11. Kurzrok, H., et al.: Endocrinology 21: 335, 1937.
12. Hamblen, E. C.: AM. J. OBST. & GYNEC. 41: 4, 1941.
13. Litzenberg, J. C.: Trans. Am. Assn. Obst. Gynec. & Abd. Surg. 41: 159, 1938.
14. Bloss, J. R.: South. M. J. 30: 637, 1937.

80 BAY STATE ROAD

DISCUSSION

DR. FREDERICK J. LYNCH, BOSTON, MASS. (By Invitation).—A discussion of the pathology of the embryo and spontaneous abortion usually includes a consideration of the condition from the point of view of the fertilized ovum, a disturbance of the endocrine or vitamin balance and a local or systemic derangement of the maternal organism.

Concerning the ovum, the most complete and comprehensive work has been done by Hertig and his associates of Boston, who have approached the subject from the viewpoint of the pathologist. They classify two groups: namely, the pathologic and nonpathologic ova, the former being those ova in which no embryo is found or in which it is extremely defective. Nonpathologic ova include those in which normal embryos are found, or in which an embryo is present with deformities which would not interfere with the development of the fetus to full term.

More than one-half of the pathologic ova spontaneously aborted showed evidence of early hydatidiform degeneration of the chorionic villi. These hydatid changes were also found in the nonpathologic ova but to a much less extent, 10 per cent (11.6). Hertig states that the cystic degeneration of the chorionic villi is due to a failure of the vessels of the chorion, which develop independently of the embryo, to anastomose with the circulation of the fetus, as a result either of the absence of the fetus or of its extreme defectiveness. The activity of the chorionic epithelium results in a collection of fluid in the loose tissue of the chorionic villus from which it is not withdrawn, if the fetal circulation is nonexistent or if it fails, and a hydatidiform degeneration results.

The lessened occurrence of hydatidiform deterioration in nonpathologic ova, spontaneously aborted, is explained by the fact that the fetal circulation has, at least, functioned for some weeks. If the usual spontaneous abortion fails to occur, these ova may continue to develop and give rise to the typical mole.

Obviously in this type of case, as Dr. Paine states, the treatment should consist of helping the uterus expel its potentially harmful contents, rather than the usual attempts to allay these efforts. Unfortunately at the present time this condition cannot be detected clinically; indeed it can only be determined microscopically, in most of the early cases, after expulsion of the uterine contents.

In the nonpathological ovum, bleeding frequently does not appear until after the death of the embryo and the abortion is incomplete. Much time and effort are spent trying to nurture a terminated pregnancy and frequently considerable expense is incurred by the futile administration of expensive hormones. Again, if the diagnosis could be accurately made that the abortion was incomplete, our efforts could be intelligently directed toward encouraging and aiding the uterus to empty itself.

An expectant policy, combined at times with endocrine or vitamin therapy, is the usual manner of handling a threatened spontaneous abortion. The present criterion for the diagnosis of incomplete abortion, in addition to the signs mentioned, namely excessive bleeding, and temperature, is the presence of fetal tissue in the dilated cervical os.

Some work is being done in an attempt to make the early diagnosis of incomplete abortion from the vaginal smear. In the vaginal epithelial cells there are observed definite changes which reflect different events that are taking place in other parts of the female generative tract. It is well known that during pregnancy there is a marked piling up or cornification of the vaginal epithelium. With the advent of parturition, there is a marked desquamation of these epithelial cells, to the point that basal cells, or pavement membrane cells, with their characteristic appearance and staining qualities appear in considerable numbers in the smears. As these cells are found only in smears from postpartal and postabortal patients (Fletcher), it is felt that their presence in a case of questionable incomplete abortion might be accepted as indicative of this condition.*

Admitting that the average patient confronted with the possibility of a spontaneous abortion would frequently prefer to wait until the ovum is partially expelled from the uterus before abandoning hope and permitting active measures to be taken to empty the uterus, the possible information derived from the smear would, at least, be of prognostic value.

It seems quite probable that some ova, from normally fertile women, are defective. Thus, if the life span of a normal ovum is forty-eight hours, the thought has been brought forward that fertilization in the last hours of this period may result in the fecundation of an imperfect ovum, with a consequent spontaneous termination of the pregnancy.

It also may be mentioned that possibly imperfect or damaged spermatozoa may succeed in fertilizing normal ova, in spite of the common chemical as well as mechanical attempts at contraception. It may happen that this union of a normal ovum and a faulty spermatozoon can be a further cause of defective pregnancy and resultant spontaneous abortion.

DR. JOHN G. WALSH, PROVIDENCE, R. I.—The most important of the varied causes of spontaneous abortion, those due to embryonic defects, has been stressed by Dr. Paine, and he has emphasized the futility of attempting any form of therapy that might prevent the expulsion of a defective ovum. It is very doubtful, however, that with any form of therapy we can prevent the expulsion of such a grossly deformed early fetus.

In any large series of abortions, there are many whose cause cannot be accurately appraised in the present state of our knowledge. We have all seen successive pregnancies result in abortion, where we have felt that the factors involved were wholly accidental. Again we see women with repeated spontaneous abortions in whom there must be a recurrent maternal factor. Malpas has estimated that such a factor is present in at least 1 per cent of all pregnant women. Irving was unable to assign a cause in 8.5 per cent of his series.

It is probable that nearly one-half of the threatened abortions will be saved by bed rest and the milder forms of sedation. Our main concern in treating such cases is to prevent uterine contractions or to allay them if they have already begun. The use of extracts of corpus luteum appears to have been more successful than any other previously available method of treatment. Falls has shown that morphia may increase rather than allay uterine irritability.

Falls and his co-workers have also shown that it is possible to determine in about 95 per cent of cases whether the fetus is still alive at the time or shortly after the patient comes under observation. If we avail ourselves of this means of diagnosis, our treatment will not have the futility that Dr. Paine implies.

Dr. Paine's skepticism regarding the value of corpus luteum extracts may be justified in view of Hamblen's recent findings. There are, however, an increasingly large number of careful studies, reporting the successful use of progesterone in recurrent abortion.

DR. JAMES R. BLOSS, HUNTINGTON, W. VA.—In the last fifteen months we have had in our private practice 34 abortions, of which 19 were the so-called spontaneous type. Of these the metabolism readings were minus in 11, plus in 2, and normal in 1. In 5 it was not possible to run a metabolism before they had aborted.

The interesting thing is that the development of these fetuses is only continued to about six weeks. The average time of abortion in those with minus tests as estimated from the last menstrual period was 14.6 weeks. In those who were minus and on thyroid therapy (11 patients), the average was 15.8 weeks. Those with high metabolic rates averaged 14.3 weeks. Those in which no test was made averaged 12.5 weeks.

There must be a deficiency in the germinal cells which has an influence in producing an abnormal child. In this respect there came under my observation, some years ago, one very interesting family with a recurring anatomic abnormality. This young couple had had two children neither of which had a pyloric opening of the stomach. It is interesting that this young man's mother had one child with the

same type of abnormality. He had a brother whose wife had been pregnant twice and each of these children presented anatomic abnormalities.

The place to start with the prevention of abortions is not after pregnancy has commenced. When examining these cases do not neglect a study of the husband, because there will be found a number of such instances in which the wife will be normal and the husband discovered to be a hypoadrenal. By treating him and securing normal spermatozoa, a successful pregnancy is secured. Several instances of this have been noted in our experience.

DR. EVAN SHUTE, LONDON, CANADA.—Mall and Meyer have been largely responsible for the opinion so widely held that most aborting embryos are abnormally constituted and that it is not advisable, therefore, to prevent their loss. Their extensive investigations were carried out about thirty years ago on specimens sent to them by physicians in the United States, Canada, and abroad. It is doubtful if these embryos represented random sampling, for only grossly abnormal formations would attract the interest of practicing physicians and be sent for study. Moreover, when we analyze the work of this famous team we find that of the first 1,200 accessions to their collection fully 353 were abnormal in structure. But only 244 of these 353 revealed embryos of any sort and, as 17 of these were in tubal pregnancies, only 227, or 19 per cent, represented deformed embryos obtained from the uterus. In short, contrary to the usual impression, it is questionable if their studies support the contention that a *random* sampling of aborted embryos would reveal a majority, or even any very high proportion, of congenital anomalies.

Only recently has the profession possessed effective agents, such as vitamin E or progesterone, with which to combat threatened abortions. All of the literature since the war has not been accessible to me, but of 224 cases reported as threatened abortion or threatened miscarriage, 184 went on under such treatment to produce living children. Of these only 6, or 3 per cent, revealed anomalies of structure. This series of 184 includes 68 of my own cases, showing three defectives, an anencephalic, a congenital heart, and a large hemangioma on the back. I also have a letter from Dr. McGonigle, the first Englishman to use vitamin E extensively in such cases, in which he mentions "about a hundred" of them with no congenital deformities ensuing. The figure of 3 per cent of anomalies in the offspring is too low to justify a *laissez-faire* policy in treating threatened abortion.

I had the privilege three years ago of discussing a paper on placenta previa read by Dr. Greenhill before this Society. At that time I mentioned that we were collecting, very tediously, a series of case histories of women who had borne previously only congenitally deformed infants. These women were treated with vitamin E, either just prior to conception or immediately thereafter, in subsequent pregnancies. Wherever possible, their husbands were also given vitamin E prior to the conception, bearing in mind the remarkable ability of vitamin E to improve deficient sperm production and quality within ten to fourteen days. The series is still too small to warrant any conclusions, but it is mentioned at this juncture for its suggestive value. We now have ten such women who have been delivered of one to three infants since the defectives were born and four more such women as yet undelivered. Of the 12 children born of these 10 mothers since the birth of the defectives, 9 have been normal. The exact data will be published later. It at least suggests that we should not throw up our hands in despair before one of the most appalling phenomena in obstetrics.

DR. FREDERICK H. FALLS, CHICAGO, ILL.—Dr. Paine's viewpoint would certainly simplify the teaching of the management of abortion. In the first place, apparently abortions are all due to defective embryos; and, in the second place, there is nothing you can do about it.

When I first used corpus luteum clinically I had difficulty in believing the apparent effects. I could not understand how a woman two to four months pregnant who had been having uterine contractions could, with an injection of a small amount of progesterone, suddenly have a cessation of uterine contractions, a cessation of the bleeding, and a continuation of the pregnancy. It was not until I put a bag in the uterus of a woman seven days postpartum, and produced good uterine contractions with pituitrin and saw these contractions stop a few minutes after using rabbit unit doses of an oily extract of corpus luteum, that I knew I had not been mistaken in my clinical observations.

When we had 41 cases studied clinically we reported them. In these 41 patients 87 per cent carried babies through to maturity and were delivered of normal babies. These women had previously lost 85 per cent of their pregnancies. One of my associates has been extending this work at the County Hospital, and we now have in a series soon to be reported about 400 cases. The percentage of recovery remains the same as in the smaller group.

Another significant fact that appeared very early in our study was that if the baby was dead in the uterus it would be expelled whether these preparations were injected or not. Also these injections will not influence uterine contractions if the woman is in labor.

As a control for this series we now have about 50 cases at the County Hospital observed within the last few months in which we have not been using the corpus luteum extract. We have allowed the patients to go along without the use of this preparation. Instead of about 85 per cent of salvaged pregnancies, we have now only between 40 and 50 per cent. Therefore it seems to me that the use of corpus luteum extract is practical and valuable in preventing abortion. In the cases in which the fetus is already dead or deformed, the probability is that it does no harm.

ENDOMETRIOSIS

WALTER R. HOLMES, M.D., ATLANTA, GA.

(From the Department of Obstetrics and Gynecology, Emory University School of Medicine)

THIS report comprises a study of the records of 145 private patients on whom a diagnosis of endometriosis was made during a ten-year period from 1930 to 1940. Although the literature on endometriosis is voluminous, comparatively few reports have been compiled based on analysis of a large series of cases. This study was undertaken with the idea that a review of the case histories, comparison of operative procedures and clinical results in a group of patients that could be carefully observed might help to clarify some of the difficult clinical problems associated with endometriosis.

MATERIAL AND INCIDENCE

The 145 patients with diagnosis of endometriosis in this series occurred among 4,763 gynecologic patients, an endometriosis incidence of 3.0 per cent. Of these 145 patients, 80 were operated upon and the diagnosis confirmed by the pathologic findings at operation and the microscopic examination of the tissue removed. The so-called hemorrhagic cysts of the ovary are not included unless associated with evidence of endometriosis elsewhere in the pelvis. All of the 80 proved cases of endometriosis were of the external or pelvic type. Adenomyosis is not included except as one of the associated pathologic lesions. These 80 proved cases of endometriosis occurred among 307 gynecologic laparotomies, an incidence of 26.0 per cent. This figure compares closely with Meigs' 32.2 per cent and Sampson's 21.8 per cent of endometriosis in all abdominal gynecologic operations.

TABLE I. INCIDENCE

Number of patients with diagnosis of endometriosis	145
Number of gynecologic patients	4763
Incidence of endometriosis	3.0%
Number of proved endometriosis cases	80
Number of gynecologic laparotomies	307
Per cent of proved endometriosis cases to all gynecologic laparotomies done	26.0

The statistical data in this paper are compiled only from the 80 proved cases of endometriosis.

AGE INCIDENCE

The youngest patient with endometriosis in this series was 22 years of age and the oldest 62. Table II shows that the greatest incidence

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

was between the ages of 34 and 38 years. In this group of cases, 78 per cent occurred between the ages of 30 and 45 years. These figures, I feel sure, do not give a true picture of the incidence of endometriosis in the earlier age groups. Severe types of dysmenorrhea and pelvic pain complained of by patients during the second decade of life may in many instances represent the early stages of this disease. In the third and fourth decades, the symptoms have become more pronounced and the lesions have advanced to a stage where diagnosis is made possible.

TABLE II. AGE INCIDENCE

AGE IN YEARS	NO. CASES	PER CENT
20-23	2	2.5
24-28	5	6.2
29-33	19	23.7
34-38	22	27.5
39-43	15	18.7
44-48	11	13.7
49-53	4	5.0
54-58	1	1.2
59-63	1	1.2
Total	80	100.0

These figures (Table II) of age incidence correspond closely with those of previously reported groups. They only serve to emphasize the tragedy of the frequency of endometriosis in young women.

LOCATION OF ENDOMETRIAL LESIONS

The distribution of the lesions of endometriosis as shown in Table III agrees with other reports in the frequency of involvement of the ovaries. One ovary was the site of 18.2 per cent of the total lesions and both ovaries 17 per cent. Therefore 35.3 per cent of the lesions occurred in the ovaries. The next most frequent site was the cul-de-sac with involvement of the uterosacral ligament area along the posterior aspect of the lower uterine segment. A high percentage of the lesions were in the rectovaginal septum diagnosed by nodules felt in this area on rectal

TABLE III. LOCATION OF ENDOMETRIAL LESIONS

ORGAN	NUMBER	PER CENT OF TOTAL ORGANS INVOLVED (164)
One ovary 30}	58	35.3
Both ovaries 28}		
Pelvic peritoneum	7	4.2
External surface of uterus	4	2.4
Rectovaginal septum	23	14.0
Bladder	2	1.2
Fallopian tubes	2	1.2
Sigmoid	3	1.8
Round ligament	1	0.6
Uterosacral ligament (with adherent rectum)	33	21.2
Uterovesical peritoneum	12	7.1
Vaginal vault behind cervix	4	2.4
Broad ligament	10	6.0
Miscellaneous (uterovesical orifice, 1; inguinal canal, 1; laparotomy scar, 1; intra-ligamentous endometrial cyst, 1; infundibulopelvic ligament, 1)		

examination. The uterovesical peritoneal fold or anterior cul-de-sac accounted for 7 per cent of the involved areas. One cannot help but be impressed by the same patterns of distribution recurring with striking frequency.

It is not the purpose of this paper to enter into a detailed discussion of the theories of the etiology of endometriosis. Since the first report in 1899 by Russell, of finding of endometrial tissue in the ovary, the work of Cullen, Von Recklinghausen, Lockyer, Novak and others have added to the sum total of our clinical knowledge on this subject. Still the riddle of the etiology of endometriosis remains unsolved. I join with others in paying tribute to Sampson for his outstanding contributions on endometriosis. Sampson's transtubal implantation theory based on careful clinical and laboratory findings is advocated by many gynecologists. However, my clinical observations have converted me to a belief in the theory of lymphatic and vascular metastasis as the mode of dissemination. Sampson himself suggested this possibility in 1922. Halban, Counseller and others have been its strong advocates. It is the only theory that satisfactorily explains the presence of endometrial tissue outside the peritoneal cavity, in the inguinal canal, lymph nodes, umbilicus, and, as has been reported by Schwarz, in the lung. Also the involved areas are so often subperitoneal and in some instances deep seated in the broad ligament and bowel wall. The theory of heteroplasia of celomic epithelium of Iwanoff, Novak and others likewise does not explain these lesions outside the pelvis or why only certain areas of the peritoneum undergo metaplasia. The theory of lymphatic metastasis will explain all the locations in which endometriosis has been described. It also seems to fit in with the clinical picture of islands of endometriosis in close proximity to the uterus in patterns of great similarity as though they followed certain definite channels in their mode of dissemination.

ASSOCIATED PATHOLOGY

In Table IV are listed the pathologic lesions associated with endometriosis in this group of patients. Fibromyomas were the most frequent lesion and were found in 53.7 per cent. Other writers have pointed out the association of fibromyomas and endometriosis. Many theories have been advanced to explain this relationship. Fibromyomas, endometriosis, and adenomyosis frequently are found in the same patient, suggesting that they may have the same etiology. They all develop in women during the menstrual phase of life. Sampson suggested that fibroids may represent the irritative reaction to a proceeding endometriosis. Adenomyosis with endometrial tissue in the center of a myomatous nodule is highly suggestive of such a theory. However, Cullen in his classical studies demonstrated extension of the uterine mucosa into myomatous tissue by direct continuity. Those who believe in the vascular or lymphatic theory of dissemination must admit that

cells from the endometrium would lodge here and there in the musculature of the uterus. Such cells might act as a stimulus to an overgrowth of fibrous and muscle tissue. Certainly external endometriosis wherever found causes a marked cellular reaction in surrounding tissues. We know that fibromyomas rarely occur in smooth muscle elsewhere in the body. On the basis of this theory the uterus is the only smooth muscle organ which might be subject to such a foreign body reaction. Repeated pregnancies might cause changes in the lymphatic channels and with long periods of amenorrhea diminish chances for such cellular metastasis. This might explain the low incidence of fibromyomas in multiparas.

TABLE IV. ASSOCIATED PATHOLOGY

	NUMBER	PER CENT
Myomas	43	53.7
Ovarian pathology		
Simple follicle cysts	20	25.0
Lutein cysts	9	11.2
Fibromas	2	2.5
Hemorrhagic cysts	4	5.0
Pseudomucinous cysts	1	1.2
Papillary cystadenoma	1	1.2
Chronic salpingitis	8	10.0
Endometrial hyperplasia	17	21.2
Adenomyosis of uterus	7	8.7
Sarcoma of uterus	1	1.2
Pelvic abscess (infected cysts)	2	2.5
Pregnancy (intrauterine)	1	1.2
Ureteral stricture and hydronephrosis	8	10.0
Kidney stone	1	1.2
Postoperative adhesions	11	13.7
Uterine retrodisplacement	23	28.7

The high incidence of follicle cysts of the ovary, 25 per cent, and endometrial hyperplasia, 21.2 per cent, might be advanced as an argument in favor of the endocrine theory of endometriosis. A recent study of Brewer and Jones would seem to discredit this theory.

Special attention should be given to the occurrence of ureteral stricture and hydronephrosis in 10 per cent of the cases. The close proximity of the ureter to the involved areas in the broad ligament and uterosacral ligament regions will frequently result in obstructive lesions of the ureters. Such a possibility should be considered in every case of endometriosis. This condition is often overlooked and will account for a residue of pain in many patients operated upon for endometriosis.

Uterine retrodisplacement occurred in 28.7 per cent. Because of its obstructive possibilities, backward displacement of the uterus is considered to be an etiologic factor. Its occurrence in 28.7 per cent of patients in this series is suggestive.

Two of the patients in this report had infected endometrial cysts. Sampson called our attention to this possibility in 1929. Due to the blood content of these cysts and their close proximity to the bowel, it is surprising that this is not a more frequent occurrence.

SYMPTOMATOLOGY

The major symptoms of the patients comprising this study are listed in Table V. This tabulation of symptoms agrees closely with reports of other authors. Certain of these symptoms will be stressed in discussion of the diagnosis of endometriosis.

TABLE V. SYMPTOMATOLOGY

COMPLAINT	NUMBER	PER CENT
Dysmenorrhea	53	66.2
Menorrhagia	25	31.2
Metrorrhagia	8	10.0
Polymenorrhea	7	8.7
Uterine bleeding (brownish discharge pre- and postmenstrual)	12	15.0
Elevation temperature leucocytosis	7	8.7
Lower abdominal pain	34	42.5
Pain inguinal region	3	3.7
Pain in thighs	8	10.0
Sacral back pains	23	28.7
Rectal pains	6	7.5
Bladder symptoms	12	15.0
Gastrointestinal symptoms	15	18.7
Upper abdominal reflex pains	5	6.1
Dyspareunia	6	7.5
Amenorrhea	6	7.5
Headache	7	8.7
Sensation of pressure in pelvis	16	20.0
Nervousness	17	21.2
Constipation and obstipation	24	30.0
Pain referred to area of kidneys	9	11.2

TABLE VI. TYPE OF DYSMENORRHEA

Pre- and intramenstrual pain	25.0
Dysmenorrhea all of menstrual life	21.1
Acquired dysmenorrhea	11.2
Premenstrual pain	15.0
Postmenstrual pain	8.7
Normal periods	18.6

TABLE VII. STERILITY

	NUMBER	NUMBER CHILDREN	STERILITY PER CENT
Single	17	0	
Married	63	29	46

The occurrence of barren marriages is recognized to approximate 12 per cent. Patients with endometriosis in this group were almost four times as sterile as the average female patient.

TABLE VIII. PREVIOUS OPERATIONS

TOTAL NUMBER OF PATIENTS	PATIENTS WITH PREVIOUS ABDOMINAL OPERATIONS	PER CENT	DILATATION AND CURETTAGE	PER CENT
80	14	17.5	5	6.2

PREOPERATIVE DIAGNOSIS

A correct preoperative diagnosis was made in 48.7 per cent of the reported cases. Among the 41 patients on whom an incorrect diagnosis was made, 26 had large fibromyomas which overshadowed the usual diagnostic findings of endometriosis (Table IX).

TABLE IX. PREOPERATIVE DIAGNOSIS (80 PATIENTS)

	NUMBER	PER CENT
Correctly diagnosed	39	48.7
Not correctly diagnosed	41	51.2

The diagnosis of endometriosis is not always easily made. Extensive lesions may exist without any subjective symptoms. Twenty per cent of my patients had menses free of pain and were normal in other respects. In no other gynecologic condition is a carefully taken history so important as an aid to correct diagnosis. The following symptoms if present in the history are of diagnostic value: (1) *Dysmenorrhea* of an acquired type, or an accentuation of pre-existing dysmenorrhea; (2) *premenstrual pain*, lower abdominal discomfort resembling menstrual cramps often of a crescendo type beginning a few days or a week or more before the onset of menstruation; (3) *abnormal uterine bleeding* in the form of menorrhagia or metrorrhagia or frequently intermenstrual brownish-colored uterine discharge; (4) *pain* in one or both lower abdominal quadrants or suprapubic areas which may be constant in character, although often its periodicity is significant (a sense of pelvic pressure described as a bearing down sensation as if everything were falling out of the pelvis); (5), *pain* referred to the groin, hip, or thighs; (6) *dyspareunia*, acquired and unexplained by other findings; (7) *obstipation* and *constipation*, often related to the time of menstruation (rectal discomfort described as a sensation that would be relieved by bowel evacuation); (8) *sterility*, unexplained after a careful sterility study; (9) *sacral backache*, menstrual type of headache, reflex gastrointestinal symptoms and bladder symptoms.

The physical findings on vaginal examination are additional aids in diagnosis. The presence of enlarged, adherent ovaries without evidence of pre-existing pelvic infection is strongly suggestive of endometrial cysts. The character of the posterior vaginal vault is of great significance. One gets the impression of a shallow posterior vaginal fornix. There is a sense of resistance and thickening of the tissue in this area. At times nodules are palpable posterior to the cervix. These nodules are more readily palpable on rectal examination with additional evidence of induration in the area of the uterosacral ligaments. Movements of the uterus are restricted. If a retrodisplacement is present, although not adherent, effort to bring the fundus forward is more difficult than in uncomplicated retroversions. Often a distinct lack of mobility of the

entire uterus is noted. This is particularly noticeable in lifting the cervix and fundus upward and forward toward the anterior abdominal wall. This fixation of the lower uterine segment accounts for the increased difficulty in mobilization of the uterus when doing a hysterectomy associated with endometriosis. There is additional evidence of unusual pelvic tenderness on vaginal examination.

TREATMENT

The treatment of endometriosis will depend on the type of symptoms, the age of the patients, the extent of the lesions, and associated pelvic pathology. It is well known that removal of all ovarian tissue will cause regressive changes in endometriomas. This may be accomplished either by bilateral oophorectomy or by irradiation. However, the frequency of endometriosis in young women presents a problem in treatment which calls for mature surgical judgment.

The treatment of endometriosis in this group of patients was mainly one of conservatism. Eighty patients were operated upon out of the 145 patients with diagnosis of endometriosis. Of these, 53 per cent had associated fibromyomas of the uterus which made surgical interference necessary. The decision for operation was based on the severity of the symptoms. Patients having endometriosis deserve a frank discussion of their condition with explanation of the cause of their premenstrual discomfort and other pelvic symptoms. Intelligent patients will endure their discomfort unless severe and prefer a status of periodic observation rather than the necessity of a mutilating pelvic operation. Observations on patients operated upon during the fourth and fifth decades of life for fibromyomas with associated endometriosis convinces me that this condition is not always a progressive pathologic lesion; that many small areas of endometriosis cause few if any symptoms and that other extensive growths have remained quiescent as a result of adhesions and inflammatory reaction about them.

There is a malignant type of endometriosis which is invasive and destructive accompanied by severe symptoms which will warrant radical treatment. In some instances extensive involvement of both ovaries makes conservation of ovarian tissue impossible.

Table X gives the types of surgical treatment in this group of patients.

The guiding principle in treatment has been relief of symptoms by removal of major lesions and if possible preservation of ovarian function. Such treatment was carried out in 80 per cent of the entire group. All of the patients in the 20 to 30 age group were treated conservatively. In 6 of the 8 patients in this age group, ovarian and reproduction functions were conserved. Necessity for reoperation or irradiation is preferable to initial radical surgery in young women. Radical surgery was carried out in 8.7 per cent of the 30- to 40-year age

TABLE X. TYPE OF SURGICAL TREATMENT (80 PATIENTS)

	AGE			
	20-30	30-40	40-50	50-62
Number of patients	8	45	21	6
Radical	0	7	5	4
Hysterectomy with conservation of one ovary	2	18	16	2
Conservative	6	20	0	0

group and 11.2 per cent in the 40- to 60-year age group. Hysterectomy with conservation of one ovary, 47.5 per cent of the patients, was the most frequent type of operation. It is generally accepted that following hysterectomy ovarian function gradually diminishes. This may account for the fact that in my patients endometriomas not entirely removed with this type of operation cause few if any postoperative symptoms. No attempt was made to remove areas of endometriosis involving the rectum or rectovaginal septum. Surgical removal of such areas is dangerous. Extensive involvement of the rectovaginal septum causing symptoms is best treated by bilateral oophorectomy. Irradiation was not used as the initial method of treatment in any of my patients. Surgery is preferred, because it gives the opportunity for conservatism with removal of large endometriomas and the correction of associated pelvic pathology.

RESULTS OF TREATMENT

There was no mortality in this series of 80 patients operated upon for endometriosis. Follow-up study was possible in 73 of the 80 patients. A conscientious effort was made to evaluate the results of treatment which are listed in Table XI. Patients following operation for endometriosis will have a greater morbidity than those following clean-cut pelvic operations due to the additional trauma and raw areas incident to the enucleation of large endometriomas. Although the relief of major symptoms in the radically treated group are excellent, one cannot help but be depressed over the high incidence of vasomotor and nervous symptoms in these castrated women. In the group with preservation of ovarian or reproductive function, only 29.1 per cent were relieved of their major symptoms. Additional irradiation treatment for relief of symptoms was necessary in 12.6 per cent of these patients. Doubtless others in this group will in time require further treatment. However, 12.6 per cent of the patients treated conservatively became pregnant, with delivery of normal babies. Two of these patients were barren eleven and twelve years, respectively, prior to operation. The number of patients is too small to draw definite conclusions as to the value of surgery in the correction of sterility associated with endometriosis. It would seem that excision of major ovarian lesions, correction of tubal adhesions, and associated retrodisplacements may increase the chances

TABLE XI. RESULTS OF TREATMENT (73 PATIENTS)

	CONSERVATIVE UTERUS AND ONE OR BOTH OVARIES CON- SERVED	CONSERVATIVE HYSTERECTOMY ONE OVARY CONSERVED	RADICAL HYSTERECTOMY BILATERAL OOPHORECTOMY
Number of patients with adequate follow up	24	35	14
Relief of chief complaints	29.1%	71.4%	85.7%
Partial relief	54.1%	25.7%	7.1%
No relief	16.6%	2.8%	7.1%
Extreme nervous symptoms	0.0%	11.4%	64.2%
Pregnancies	12.6%	0.0%	0.0%
Subsequent treatment			
Irradiation	12.6%	0.0%	0.0%
Surgery	0.0%	0.0%	0.0%

for conception in some patients. Hysterectomy with preservation of some ovarian tissue seemed to give the best end results in this series of patients.

SUMMARY

1. Eighty patients with proved endometriosis occurred in 307 gynecologic laparotomies, an incidence of 26 per cent.

2. Endometriosis is a disease of middle menstrual life with an incidence of 78 per cent between the ages of 30 and 45 years in the reported group of cases.

3. The majority of the endometrial lesions occurred in the ovaries, anterior and posterior cul-de-sac, and the rectovaginal septum.

4. The frequent occurrence of external endometriosis, adenomyosis, and fibromyomas in the same patient suggests that these may have the same etiology. Belief in the theory of vascular and lymphatic metastasis as the mode of dissemination of endometriosis is expressed.

5. Dysmenorrhea, abnormal uterine bleeding, lower abdominal pain, sacral backache, and dyspareunia are the most frequent symptoms of endometriosis.

6. Conservatism in the treatment of endometriosis is justified by the end results in the cases reported.

7. Endometriosis with its riddle of etiology, its devastating effects on the reproductive organs of young women, its unknown factors of prevention remains a real challenge to every gynecologist for the solution of these problems.

REFERENCES

1. Russell, W. W.: Bull. Johns Hopkins Hosp. 10: 8, 1899.
2. Cullen, T. S.: Adenomyoma of the Uterus, Philadelphia, 1908, W. B. Saunders Co.
3. Sampson, J. A.: Boston M. & S. J. 186: 445, 1922.
4. Sampson, J. A.: Arch. Surg. 5: 217, 1922.
5. Halban, I.: Wien. Klin. Wchnschr. 37: 1205, 1924.
6. Sampson, J. A.: Am. J. Path. 3: 93, 1927.
7. Sampson, J. A.: AM. J. OBST. & GYN. 18: 1, 1929.
8. Keene, F. E., and Kimbrough, R. A.: J. A. M. A. 95: 1164, 1930.

9. Novak, E.: *AM. J. OBST. & GYNEC.* 22: 826, 1931.
10. Hill, L. L.: *Am. J. Surg.* 18: 303, 1932.
11. Hansmann, G. A., and Scheken, J. R.: *AM. J. OBST. & GYNEC.* 25: 572, 1933.
12. Schumann, E. A., and Parke, W. E.: *AM. J. OBST. & GYNEC.* 28: 222, 1934.
13. Meigs, J. V.: *Surg., Gynec. & Obst.* 67: 253, 1938.
14. Dougal, D.: *AM. J. OBST. & GYNEC.* 35: 373, 1938.
15. Schwarz, O. H.: *AM. J. OBST. & GYNEC.* 36: 887, 1939.
16. Long, W., and Strecker, W. E.: *South. M. J.* 32: 489, 1939.
17. Counseller, V. S.: *AM. J. OBST. & GYNEC.* 37: 788, 1939.
18. Fallas, R., and Rosenblum, G.: *AM. J. OBST. & GYNEC.* 39: 964, 1940.
19. Payne, F.: *AM. J. OBST. & GYNEC.* 39: 373, 1940.
20. Allen, E.: *J. Lancet* 60: 114, 1940.
21. Henderson, D. N.: *AM. J. OBST. & GYNEC.* 41: 694, 1941.
22. Dannreuther, W. T.: *AM. J. OBST. & GYNEC.* 41: 461, 1941.

478 PEACHTREE STREET, N. E.

DISCUSSION

DR. A. D. CAMPBELL, MONTREAL, CANADA.—The incidence of endometriosis in the experience of most of us is that observed by Dr. Holmes. These figures are conservative and represent only those cases with more or less active endometriosis. In many instances the condition may exist in subclinical form and be labeled as post-operative adhesions.

Often, upon opening the abdominal cavity, one encounters scar tissue at the junction of the broad ligament with the uterus or along the uterosacral ligaments or as dense adhesions fixing the lower part of the sigmoid to the peritoneal surface of the vaginal vault. Certain as one may be that the etiology of such scars is a sequel to endometriosis, one cannot prove this point in the absence of histologic evidence. If nonactive or healed endometriosis were added to active endometriosis, the incidence of this condition would mount considerably.

At this point may I suggest that the term "dysmenorrhea" be less promiscuously used than at present. In 1926 Sir Henry Beckwith Whitehouse suggested restricting the term "dysmenorrhea" to embrace a certain symptom complex and that pain associated with menstruation be termed "menorrhagia." I subscribe to this differentiation.

No one theory of etiology of endometriosis is applicable to all cases. In endometriosis of the vulva and the umbilicus one does not need, however, to seek special theories when one can demonstrate a patency in the canal of Nuck or a scarred hernial tract extending from the abdominal cavity into the umbilicus. In this connection I have had the opportunity to dissect carefully the umbilical area in cases of ectopic gestation presenting so-called Cullen's sign. I have carried out similar dissections on endometriosis of the umbilicus and found scar tissue which undoubtedly was the remains of the small hernial canal through which transplants escaped from the abdominal cavity.

The treatment of every case must be judged in the light of its particular circumstances. Were it not for the fact that the life history of endometriosis is problematical and that the process becomes so arrested that in rare cases pregnancy has followed, one would have grounds for the most radical treatment in all cases of endometriosis. In general, however, in no case where endometriosis has spontaneously developed will a patient become pregnant so long as endometriosis remains active.

When marked endometriosis involves the rectovaginal septum, I feel that pan-hysterectomy with complete resections of the ovaries is wise, for here, probably more than in any other location, is malignancy likely to be superimposed upon this lesion. In either the conservative or radical surgical treatment of endometriosis one must at operation completely peritonize all raw areas. Where the pelvic peritoneum is destroyed, I strongly suggest peritonization by a form of marsupialization

of this area. The patient is then left with a completely peritonized pelvic basin. Where one is more conservative, in addition to this precaution, it has been my practice for years to perform a presacral sympathectomy. By so doing one may with confidence be less radical and leave the patient with at least some ovarian tissue. One, too, can reassure the patient that she will in all probability be free from pain.

Endometriosis will not be completely understood, either from the standpoint of etiology, of its life history, or its sequelae, until we understand more clearly the relationship between ovarian function and that of the endometrium. I am firmly convinced that endometriosis is primarily an endocrinologic problem. Experience has clearly demonstrated to me that in certain instances sterility, endometriosis, and ectopic gestation are due to the same endocrinologic influences.

DR. JOE V. MEIGS, BOSTON, MASS.—In May, 1941, I reported that in my private practice of 400 patients with gynecologic conditions necessitating abdominal surgery, 28 per cent had endometriosis; 112 out of 400. In the same period of time at the Massachusetts General Hospital, of 400 patients necessitating abdominal surgery only 5.8 per cent had endometriosis. In private practice there is, therefore, much more endometriosis than in a charity hospital practice.

Endometriosis is not a true tumor but a physiologic response to an abnormally uninterrupted menstrual career. Patients should not menstruate as often as they do without an intervening pregnancy. I think that because of the economic trends of the times we are allowing women of the private patient class to go too long without a pregnancy. That is the whole crux of the endometriosis situation. Stimulation by something (estrin) is causing the celomic epithelium to grow.

I believe we must change our ideas and instead of leaving an inheritance to our daughters when they reach about 50 years of age, we should encourage them to marry when young, at 18 or 21, and help them financially then instead of waiting until they are older.

I believe that delayed pregnancies are responsible for this entity. If endometriosis commences, fertility is immediately lowered. In my private practice, the fertility of patients with endometriosis was 65 per cent as against 90 per cent in those that did not have endometriosis. Fifty per cent of the patients I have operated upon since June have had endometriosis. There must be something wrong somewhere.

DR. WILLARD R. COOKE, GALVESTON, TEXAS.—In the clinical diagnosis I find a rather valuable guide in the development of a new type of dysmenorrhea superimposed upon the previously existing type. If we study these cases carefully, this dysmenorrhea is found to be of the peritoneal type. By recognizing this symptom the percentage of accurate diagnosis is increased.

As to treatment, the young individual in whom reproduction is essential must be relieved of a very real pain. For that I have found very useful the operation of presacral sympathectomy, combined with bilateral ovarian neurotomy. In our group of cases so treated, a perfectly normal menstrual cycle has been resumed after the initial menorrhagia of from one to three cycles. I have done this operation on 5 individuals of whom 3 have since become pregnant. One patient with a periureteral infiltration was not affected by the presacral sympathectomy, and was elsewhere given a subcastration x-ray treatment. She became pregnant and aborted, the fetus having a central nervous defect.

I am in thorough accord with Dr. Meigs' remarks. There is something in the mode of life in the so-called higher classes which accounts definitely for 80 per cent of their functional disturbances. Ninety per cent of the psychoneuroses come from the same source which is reflected in gynecologic symptomatology.

DR. JAMES R. GOODALL, MONTREAL, CANADA.—Endometriosis is a general pelvic disease operating from a general pelvic cause, and it is a mistake to separate

endometriosis into various subdivisions. All forms of endometriosis arise from the endometrium, but it is very important to find out from what part of the endometrium the endometriosis has taken its origin. It is known, of course, that when the endometrium responds to the menstrual cycle only the surface layers are affected. If endometriosis has arisen from cells desquamated from the surface of the endometrium, by the "spill" method, we invariably get chocolate cysts because these cells respond to the hormones of the menstrual cycle. On the other hand, if the endometriosis starts from the basal layer of the endometrium, it does not respond to the cycle of menstruation as it penetrates the uterine wall.

The methods of extension of endometriosis are in every way analogous to the methods of spread of infection. In my textbook on *Puerperal Infections* I stated that the extension of the disease was by one of four methods: First, that the extension was local; second, that it extends by the blood vessels; third, by the lymphatics; and fourth, by surface continuity out of the tubes, and so it is with endometriosis.

If we examine all of the organs of the pelvis in endometriosis, we find various correlated lesions which otherwise would not have been recognized except by biopsy. One example is the hypertrophy of the uterine musculature which is a response to the menstrual cycles. We have, however, also found a new disease which is correlated with endometriosis, although sometimes found independently, and that is peritoneal sclerosis. Oftentimes when opening the abdomen I have diagnosed endometriosis, when I had not suspected it, by the thickness of the peritoneum, in some cases so thick that when the scissors go through the vesicouterine fold it gives a sound like cutting through cartilage.

There is but one common cause of endometriosis. I am more convinced than ever that endometriosis is an expression of hyperestrinism. I do not think this will ever be demonstrated conclusively, because hyperestrinism may be of two types, an absolute hyperestrinism or a relative one. If I give a patient a very large dose of estrogen and examine the urine in the next twenty-four to forty-eight hours, I may recover very little of it, but if I follow with a dose of progesterone, an increase in estrin excretion is noticeable almost immediately. That proves, I think, that there is a chemical combination between estrin and the endometrial cells although an examination of the blood or urine would not show any degree of hyperestrinism.

I was delighted to hear Dr. Meigs' remarks about sterility. In my recently finished book on *Endometriosis* I advocated exactly what Dr. Meigs has advocated today. Not only should our young girls marry earlier but they should have several children. The nulliparous married woman is just as susceptible to endometriosis, however, as the unmarried young girl.

I have had an eye opener in the last year. We have been studying the relation of the ovary to pregnancy and have found that the ovary ceases to function at about the sixth month of pregnancy. From that time on it resembles very much the ovary of a senile woman. We have traced that through the later months of pregnancy and through the puerperium. If you remove the ovaries of a woman immediately after her first menstruation following pregnancy it will show the most astounding picture. The ovary ripens anywhere from 4 to 12 ova all at once to bring about that menstruation and the regeneration of all the pelvic organs, notably the uterine musculature. This supplements what Dr. Meigs has said. I think that there we are touching on something which is absolutely vital and that endometriosis is the result of our so-called civilization.

MANAGEMENT AND OUTCOME OF LABOR IN 742 WOMEN WITH BORDERLINE PELVES*

J. BAY JACOBS, M.D., F.A.C.S., WASHINGTON, D. C.

(From Georgetown University School of Medicine and the Department of Maternal
Welfare, Health Department)

THE study of this particular group of women classified as having borderline pelves, was begun July 30, 1936, and terminated Aug. 1, 1941, a period of five years. All of them were indigent and received prenatal care from the Health Department of the District of Columbia. Their relative frequency may be stated as one-twelfth of the entire clinic attendance during the five-year period.

Probably the most important mechanical factor in obstetrics is the pelvis. Where a large number of patients and many clinicians are involved, it is necessary to adopt certain standards of recognition for borderline and contracted pelves. For further observation and x-ray study, patients in such category may then be referred to the "abnormal" clinic, which is conducted by a single individual.

It is essential to recognize pelvic contraction, and for that reason we had established a broad standard of selection, which would include almost any case of potential danger. Thus all primiparas with a diagonal conjugate diameter of 11.5 cm. or less, and all multiparas with a diagonal conjugate of 11 cm. or less, regardless of previous history of childbirth, have been referred to the x-ray clinic.

The diagonal conjugate was measured on the Douglas pelvimeter. In the 760 cases that ranged from 8.5 to 11.5 cm., the actual length of each diagonal conjugate, the frequency, and color incidence are shown in Table I.

My technique of lateral pelvic roentgenography in which film scales are used to measure films¹ was selected for the study of these patients, because of its inexpensiveness, simplicity, and accuracy. By this procedure the degree of engagement of the fetal skull is readily noted, and disproportion when present may be recognized. All the important landmarks of the pelvis are readily identified, and the true conjugate diameter, extending from the middle of the upper border of the symphysis to the sacral promontory, is unmistakable.

What the author refers to as the *available true conjugate diameter* extends from the posterior surface of the symphysis to the sacral

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

TABLE I

D.C.	TOTAL	WHITE	COLORED
8.5	2		2
8.8	1		1
9.0	3		3
9.5	6	1	5
9.8	1		1
10.0	29	4	25
10.3	8	1	7
10.5	57	4	53
10.8	30	1	29
11.0	345	40	305
11.1	1		1
11.3	25	3	22
11.4	1		1
11.5	251	28	223
Total	760	82	678

promontory; this is about 7 mm. less than the true conjugate. In this study, all references are made to the true conjugate, since that is the custom of most authors.

DIAGONAL VERSUS TRUE CONJUGATE

In a previous study,² it was shown that Smellie's rule of subtracting 1.5 to 2 cm. from the diagonal to obtain the true conjugate applied in 8 per cent of cases; and in 89.5 per cent the difference between these two diameters was less than 1.5 cm. I also mentioned the existence of pelves in which the length of the true conjugate approaches and even exceeds that of the diagonal; and in the present study I have found several such. If the true conjugate were not measured with precision, but merely estimated by Smellie's rule, some of the patients with ample inlets would probably have been subjected to cesarean section.

At present I am reporting on 760 borderline pelves in which a comparison between the diagonal and true conjugates could be made. Of these women 678 were colored and 82 were white; 497 were primiparas and 263 were multiparas.

The true conjugate diameters, not estimated, but actually measured, varied from 7 cm. to 14.5 cm. *There is no constant relationship between the diagonal and true conjugates.* The most common true conjugate in 760 cases was 10 cm.; this was found 68 times.

For any particular diagonal conjugate, there may be a wide variation of true conjugates. Reference is made to a few examples:

In two cases where the diagonal conjugate measured 8.5 cm., the true conjugate was 7 cm. in one and 10.4 cm. in the other. One of course required cesarean section and the other did not.

In 30 cases, a diagonal conjugate of 10.8 designated a true conjugate varying between 8.4 and 11.5.

There were 25 patients with a diagonal conjugate of 11.3. Here the true conjugates varied between 9.2 and 12 cm.

Of the 760 cases, the diagonal conjugate exceeded the length of the true conjugate in 443. The two diameters were equal in 56 women; and in 261, the diagonal conjugate was smaller than the true conjugate.

For a long time, I have directed attention to the variable relationship between these two important diameters. My original observations were made with the "obstetric inclinometer"³ and the findings have been repeatedly confirmed in my roentgen pelvimetric studies. Variability in size, of what I have called *the obstetric angle*, accounts for the varied relationship in different women. By the obstetric angle is meant the angle between the symphysis and diagonal conjugate diameter. It is readily seen that a wide angle will include a large true conjugate, and an acute angle will subtend a short one. By the use of pelvic roentgenography, this information is readily obtained, without mathematical calculation.

It was noted also, that

1. Seventy-nine cases, or 10.4 per cent, conformed to Smellie's Rule.
2. In 16 women, or about 2.1 per cent, the true conjugate was more than 2 cm. less than the diagonal. In this group of course the prognosis is least favorable, depending upon the length of the diagonal conjugate diameter.
3. There was a group of 665 women, or 87.5 per cent, in which the length of the true conjugate varied between 1.4 cm. less to 3.4 cm. more than the diagonal. Naturally, patients falling into this large group are benefited by a more favorable prognosis.

These observations check to a remarkable degree with the findings in the small series of 80 cases already referred to, in which the proportions were, respectively, 8 per cent, 2.5 per cent, and 89.5 per cent.

Unfortunately, statements by authorities, relative to the management and outcome of labor in borderline pelves, have not been based upon accurately determined true conjugates, but upon those estimated with the use of Smellie's Rule.

One may realize the false concepts that might have been arrived at in the present series of cases had they been managed by merely measuring the diagonal conjugate and applying Smellie's Rule, instead of using x-ray to measure the true conjugate. Suffice it to say, that treatment would have been much more radical, not individualized, and the results less favorable than this study will show.

The work here presented has been particularly interesting to me because of the manner in which it was conducted. I have had an opportunity to examine all of the patients; I have taken an active part in the roentgenography of each of them, interpreted the films, read the measurements, predicted the prognosis and advised treatment. All were followed from the prenatal clinic through delivery.

COMPARISON OF PROGNOSIS AND OUTCOME

This was possible in 742 cases out of the 760, since 18 had not delivered.

Prognosis was based upon interpretation of film; in multiparas some consideration was given to previous childbearing.

In my opinion, when prediction of prognosis is greatly influenced by roentgenographic findings, as is my custom, the effect of color is not as important as had been heretofore considered. For we are able not only to measure the head and pelvis, but also to note cephalopelvic relationship.

Of course, where one does not employ this procedure, his judgment must be influenced by all other less dependable facts and theories.

Prognosis was stated as follows:

1. Favorable
2. Guarded
3. Test labor
4. Probable cesarean section

In every case the predicted prognosis and suggested method of treatment were recorded and sent to the person or hospital responsible for delivery, before the onset of labor.

Table II represents clearly the comparison between prognosis and type of delivery or outcome in this particular series. Although it should not be followed as a guide, it shows that lateral pelvimetric study may have a conservative effect upon the conduct of the obstetrician, as well as enable him to predict prognosis with some degree of precision.

TABLE II. PROGNOSIS

Prognosis was predicted as favorable, guarded, test labor, and cesarean section. Under each of these four headings is found the number so predicted. Reading across the page gives the number of each type of delivery in each of the four groups.

	TOTAL	FAVOR- ABLE	GUARDED	TEST LABOR	CESAR- EAN SECTION
Total	742	494	82	144	22
Normal	580	413	54	108	5
Forceps	99	64	13	20	2
Cesarean section	46	8	11	13	14
Breech extraction	12	6	3	3	-
Version and extraction	4	2	1	-	1
Craniotomy	1	1	-	-	-

1. A favorable outcome was predicted in 494 women. What actually happened in these cases was as follows: 413 delivered normally; 64 were forceps deliveries, mostly prophylactic; 6 breech extractions; 2 version and extraction; 1 craniotomy on a dead hydrocephalic baby; and 8 cesarean sections which will be accounted for under the heading "Analysis of Cesarean Sections."

2. The prognosis was considered guarded in 82 cases. Fifty-four of these delivered normally; 13 were delivered with forceps, 3 by breech extraction, 1 by version and extraction, and 11 by cesarean section.

3. Test labor was advised in 144 women. One hundred and eight of these delivered normally, 20 were delivered with forceps, 3 by breech extraction, and 13 by cesarean section.

4. Probable cesarean section was the prognosis predicted in 22 women. Only 14, however, were so delivered.

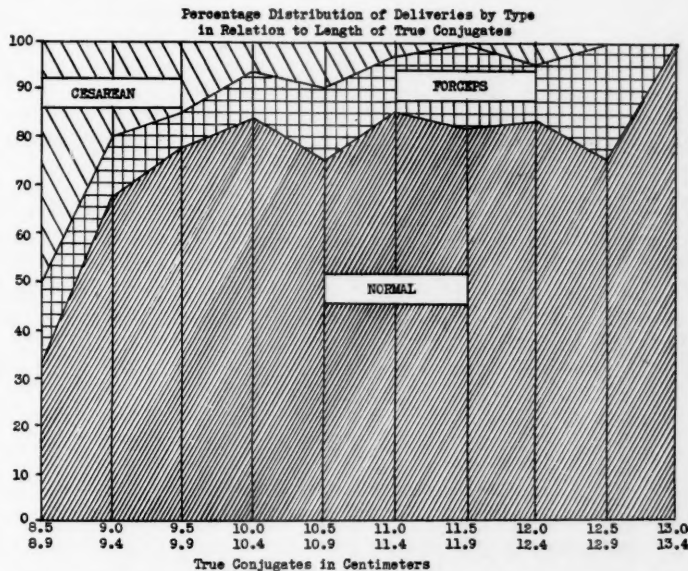


Fig. 1.—Diagonal conjugates below 8.5 cm. are not represented in this graph because the exceedingly small number of cases would probably create a false impression. Likewise diagonal conjugates of 13.5 cm. and over are omitted because under ordinary circumstances all cases in this category should deliver normally.

Breech, version, and extraction and craniotomy are omitted because the relatively few cases in these groups would merely confuse the graph.

The expectation for normal delivery improves as the size of the true conjugate increases. Of course cesarean sections done for reasons other than pelvic contraction, as well as prophylactic forceps, do interfere somewhat with the above expectancy.

TYPE OF DELIVERY

According to type of delivery, the 742 borderline cases were distributed as follows:

Normal	580, or 78.2 per cent
Forceps (including prophylactic)	99, or 13.4 per cent
Cesarean section	46, or 6.2 per cent
Version and extraction	4, or 0.5 per cent
Breech extraction	12, or 1.6 per cent
Craniotomy	1, or 0.1 per cent

ANALYSIS OF CESAREAN SECTIONS IN THE FOUR GROUPS

1. *Favorable.*—In this group of 494 women, there were 8 cesarean sections; an incidence of 1.6 per cent. One operation was done because

of a large fibroid; 2 because of previous cesarean section; 1 for placenta previa; 1 was twins, probably not diagnosed; and in the other 3, there was no engagement after long labor.

2. *Guarded.*—Out of 82 cases, there were 11 cesarean sections, an incidence of 13.4 per cent. Four of the operations were done because of breech presentation in marked borderline pelvis.

3. *Test Labor.*—In 144 cases there were 13 cesarean sections, an incidence of 9 per cent.

Two were done because of previous cesarean section; 1 because of previous difficult labor; 1 for breech presentation in a primipara; and 1 for impacted transverse presentation. There were 5 sections done without adequate test labor. The remaining 3 did have adequate test labor.

4. *Probable Cesarean Section.*—Out of 22 such patients, only 14 were sectioned; an incidence of 63.6 per cent. Of the other 8, 5 delivered normally (of which 1 was premature), 2 were delivered with forceps, and 1 by version and extraction. This group shows the greatest discrepancy between prognosis and outcome; such error tends toward conservatism.

If an occasional patient had not delivered prematurely, and if some had not been sent for x-ray too early in pregnancy, the prediction of prognosis, particularly in this group, might have been more accurate.

TYPE OF DELIVERY THAT OCCURRED IN PELVES OF ACCURATELY DETERMINED
TRUE CONJUGATES OF VARIOUS LENGTHS

It will be noticed that the incidence of each type of delivery is quoted for every half centimeter variation in the length of the true conjugate diameter. The percentage frequency is shown in the graph, while numerical frequency is stated in Table IV.

TABLE IV

		NORMAL	FORCEPS	CESAR- EAN SECTION	BREECH	VERSION AND EXTRAC- TION	CRANIOT- OMY
True Conjugate	7.0- 7.4	-	-	1	-	-	-
	7.5- 7.9	1	-	1	-	-	-
	8.0- 8.4	2	1	1	-	-	-
	8.5- 8.9	2	1	3	-	-	-
	9.0- 9.4	27	5	8	-	-	-
	9.5- 9.9	56	6	10	1	1	-
	10.0-10.4	122	16	7	3	-	-
	10.5-10.9	90	20	10	3	1	-
	11.0-11.4	122	16	3	1	2	-
	11.5-11.9	88	19	-	3	-	-
	12.0-12.4	42	6	2	1	-	1
	12.5-12.9	18	6	-	-	-	-
	13.0-13.4	7	-	-	-	-	-
	13.5-13.9	2	2	-	-	-	-
	14.0-14.4	1	-	-	-	-	-
	14.5-14.9	-	1	-	-	-	-

Similarly, the type of delivery according to length of diagonal conjugate is known but not stated, because the diagonal conjugate is a false index for prognostication. One cannot surmise the length of the true conjugate from the diagonal.

MATERNAL MORTALITY AND STILLBIRTHS

There was one maternal death. This patient died twenty-six days after a normal delivery. She was an old rheumatic and cause of death was acute bacterial endocarditis.

There were only 9 stillbirths. Four were macerated and the mothers had syphilis. The mother of one had pneumonia. The mother of another had pre-eclamptic toxemia. One was an impacted transverse presentation. One had a craniotomy. In one the cause of death was not determined.

SUMMARY

In the prenatal clinics of the Health Department of the District of Columbia the incidence of borderline pelves was one-twelfth of the entire registration, over a five-year period.

The results of roentgen measurements indicate that Smellie's Rule should be discarded.

The lateral pelvic roentgenogram was the most important factor, governing treatment in these women; 78.2 per cent of them delivered normally; 13.4 per cent were delivered with forceps. Cesarean section was performed in 6.2 per cent; some sections were done for causes other than pelvic contraction.

Of the 742 cases, a favorable outcome (meaning by favorable outcome a normal delivery or average forceps) was predicted in 494. Almost 477 were so delivered, since there were some difficult forceps deliveries.

The degree of correct prognostication and the moral support obtained from the lateral roentgenogram have been very gratifying to the author, and have been of definite assistance to those performing the deliveries.

Grouping pelves according to true conjugates that are obtained by Smellie's Rule, and thus directing treatment, which is the conventional method, is unscientific and misleading.

CONCLUSIONS

1. It is significant that no reference has been made to modern pelvic classifications denoting types. Likewise, reference to anteroposterior roentgenography has been avoided.

From the point of view of management, mere classification of pelves is of less value than the lateral pelvimetric roentgenogram except where marked distortion or where some very unusual departure from normal structure exists.

As regards the anteroposterior roentgenogram, it is of definitely less value than the lateral. It is of aid in measuring transverse contraction of the inlet, but such contractions that are marked enough to prevent engagement are extremely rare. None was encountered in this series.

2. For practical purposes the author regards pelves as normal, borderline, or absolutely contracted.

What to do with the normal and definitely contracted ones is generally known.

3. Borderline cases may be detected by referring every primipara with a diagonal conjugate of 11.5 cm. or less and every multipara with a diagonal conjugate of 11 cm. or less, for a lateral pelvic roentgenogram, preferably late in pregnancy.

Mensuration and interpretation of the film will establish sound basis for forming an opinion; this is an intelligent method of approach.

It not only will help to decide whether to give a patient a test of labor, but in correlation with the character of the labor, will afford some idea as to how much of a test is warranted.

Cooperation is gratefully acknowledged to the Staff of Dr. George C. Ruhland, Health Officer, for the analyses involved in this study.

REFERENCES

1. Jacobs, J. Bay: AM. J. OBST. & GYNEC. 40: 1, 150, 1940.
2. Jacobs, J. Bay: AM. J. OBST. & GYNEC. 33: 5, 778, 1937.
3. Jacobs, J. Bay: AM. J. OBST. & GYNEC. 15: 5, 689, 1928.

WASHINGTON MEDICAL BUILDING

DISCUSSION

DR. SAMUEL A. COSGROVE, JERSEY CITY, N. J.—Dr. Jacobs follows the rule of most authors in designating the anatomic conjugate of the inlet as the true conjugate, although he recognizes and emphasizes the importance of the obstetric conjugate or what he calls the "available" true conjugate. There is some disparity of practice in relation to these terms. One of the most important uses of lateral pelvic roentgenography is the ability which it gives us to determine accurately the obstetric or available conjugate. Inasmuch as either end of this diameter is a variable, we have in the lateral x-ray for the first time the means of its accurate determination. In our own clinic, it is this conjugate which we endeavor to estimate as a basis for prognosis and think of it as the true conjugate.

I concur with Dr. Jacobs in the invalidity of Smellie's formula. We have noted in our own work, however, a very much closer correspondence between the clinically observed length of the diagonal conjugate, and the roentgenographic estimation of the available conjugate, than has heretofore been recognized in ordinary pelvimetric practice. In the majority of cases the difference does not exceed half a centimeter.

I also agree with Dr. Jacobs that if one were compelled to depend on one x-ray film, the transverse plate would be the most useful. I do not agree with him, however, that a wholly competent roentgenographic study of the pelvis can be made with such films. In our own practice we include such films in our pelvic roentgenographs, but use instead of Dr. Jacobs' screens, a modification of the Weitzner rule which our own x-ray laboratory has devised. This has the advantage of permanently including in every film a means of direct measurement.

We also use stereoroentgenographs of the pelvic inlet and of the outlet, for it does not seem to us that prognosis can be entirely predicated upon the length of the AP diameter and the inclination of the pelvis, on which Dr. Jacobs appears to depend. The configuration of the inlet is to us important. It seems self-evident that between any two pelves with the same true conjugate, the prognosis might vary considerably if one presented a typical android inlet, the other a typical anthropoid

inlet. Moreover, we wish to include in our prognosis not only the question of engagement and descent of the head through the inlet, but also potential difficulties in the midplane and at the outlet. We feel that in order to do this properly, films in two other planes must be correlated to those taken in the transverse aspect of the pelvis.

The real accuracy of prognosis is particularly hard to estimate. For instance, in Dr. Jacobs' first group of 494 women, 477 delivered "favorably," that is, either spontaneously or by "ordinary" forceps. One might wonder what is embraced in the term "ordinary" forceps, and exactly what the indications and conditions were in those cases so delivered but not included in the number which were "mostly prophylactic." For completion of the whole statistical picture, it would be interesting also to know what happened to the more than 90 per cent of Dr. Jacobs' total material which was not subjected at all to this careful type of x-ray prognosis. They should all, of course, have been expected to deliver "favorably."

I find that in 1,000 consecutive cases selected at random of full-term deliveries on our service, the vast majority of the patients had not been subjected to critical estimation and prognosis, 93.6 per cent delivered either spontaneously or by forceps, as compared to 96.5 per cent of the group in Dr. Jacobs' series who had been most carefully determined as presenting wholly favorable prognosis.

The difficulty of estimation for accuracy of prognosis becomes greater in relation to the equivocal groups of Dr. Jacobs' classification. In the second group the prognosis was considered guarded. This might be paraphrased by saying that possible trouble was expected in them. Was the prognosis accurate in the 54 of the 82 which escaped this possible trouble or in the 28 who actually encountered trouble? In his third group in which "test labor" was advised, the prognosis might be stated in other terms to represent the probability of trouble. Again, was the prognosis accurate in the 108 who escaped trouble or in the 36 who actually ran into trouble? I do not want to belabor this question. It is, after all, not especially important; yet as nearly as I am able to compute it, Dr. Jacobs has been accurate in 88 per cent of the prognoses of all his cases. In our own work we are not able to credit ourselves with accuracy of prognosis in much over 80 per cent. However, the percentage of accuracy is not a measure of the value of this work. The provision of data and the furnishing of warning signals to the men responsible for the eventual conduct of the labor in these cases is all that we may hope to accomplish. In the last analysis, management must depend on the judgment of the individual under whose observation the actual labor performance takes place.

DR. WILLIAM T. McCONNELL, LOUISVILLE, KY.—A great many babies are lost because of our inability to determine accurately the relative proportion between a given baby and a given pelvis at a given time. In practically every paper on cephalopelvic disproportion emphasis is laid on the estimation of pelvic diameters and types of pelves. But I have yet to hear or read a paper setting forth any practical method of determining the relation between the size of a given head and the pelvic capacity of the mother at the time of delivery.

We must bring this thought into our work and into our teaching. It is not a question of how big the pelvis or the baby may be, but of how that baby's head matches up with that pelvic capacity at that particular time. The average roentgenologist is of very little help, for his report usually reads something like: "Baby apparently at full term; apparently no cephalopelvic disproportion." Men doing obstetrics should familiarize themselves with some particular method in their prognostication of what is going to happen to that woman and that baby. For example, in cases where the lead is low in the pelvis and freely movable at term, we are justified in believing that that baby will be delivered spontaneously or with ordinary forceps.

If I were limited to only one x-ray picture I would certainly prefer the lateral view. One reason is that you get a better view of the pelvic inclination, as Dr. Jacobs has frequently mentioned. Another reason is that the head is in practically the same plane as the true conjugate, so that you do not have the distortion due to differences in magnification, on account of the distance from the x-ray machine to the plate.

Obstetrical patients fall into one of three classes: One, the cases where we can see at a glance that there is plenty of room; another, where we can see from the x-ray examination that it is a questionable case; and third, the cases in which we can tell definitely that there is marked disproportion. In the cases where there is plenty of room and in those with marked disproportion, we need have little concern about what to do. It is to the group with relative disproportion that thought must be given. It is very simple to take an ordinary lateral plate and with the centimeter rule measure the longest diameter of the head and the true conjugate. If the outlet is normal and you have from 1 to 3 cm. less on the long diameter of the head than you do on the true conjugate, you can feel sure that everything is all right.

DR. A. N. CREADICK, NEW HAVEN, CONN.—This paper establishes the fact that the old-fashioned external measurements, and even the true conjugate, are of limited value as compared with such facilities as are here described. The lateral film does not, of course, preclude the use of other films. This film, for example, does not permit a study of asymmetrical contractions of the inlet.

The exact technique employed is not important, but the point is that the obstetrician must at once get in touch with his x-ray technician and work out a simple means of performing these examinations. These are done, not to eliminate abdominal palpation, and the other examinations, but to serve as an adjunct to them. With the lateral view alone, the passageway is not completely pictured, but Dr. Jacobs has done remarkably well in calling your attention to the various interesting minor variations that play such an important part in the function of that passageway.

DR. JACOBS (closing).—Dr. Cosgrove shows more concern regarding pelvic classification and the use of stereoroentgenograms than I do. Although it must be conceded that these factors are of value, in my mind they are not as practical, from the point of view of expense and routine application, as the procedures I have advocated. I have in particular directed attention to what may be done with limited finances and facilities, such as exist in any large clinic, and the favorable results obtained.

We realize that the "available true conjugate" which is 0.7 cm. less than the true conjugate, is the determining diameter as far as engagement is concerned. Yet this was not emphasized in the manuscript, because all authors and almost all clinicians use for both reference and comparisons the true conjugate.

Dr. Cosgrove stated that the prediction of prognosis in the "guarded," "test labor," and "cesarean section" groups was not specific as in the "favorable" group. In this respect I would reply that the percentage of accuracy in prognosticating is not the ultimate purpose of such study. The idea is to classify the case in the appropriate group so that the patient can receive proper consideration.

Of course there are other factors, as suggested by Dr. Creadick, that are important, such as type of uterine contractions, behavior of cervix, etc. But I still think that the most important factor is the bony pelvis, and usually the most important part is the plane of the inlet, and the most important diameter is the true conjugate.

Although the application of roentgenographic study is an adjunct to obstetric management, it is as far as I know the most important one that we have, and is particularly intended for borderline cases.

This presentation was prepared for three purposes:

1. To show that Smellie's rule is invalid.
2. To emphasize that roentgenographic interpretation, by a simple technique, should be available in all borderline cases.
3. To show that the vast majority of borderline cases, if properly studied, may be treated conservatively.

OCCIPUT POSTERIOR—A NORMAL PRESENTATION*

L. A. CALKINS, M.D., PH.D., KANSAS CITY, KAN.

(From the Department of Obstetrics and Gynecology, Kansas University Medical School)

IN A PREVIOUS publication,¹ I stated that occiput posterior occurs almost as frequently as occiput anterior. It does not produce a significant increase in either maternal morbidity or fetal mortality. Spontaneous internal rotation can be as confidently expected in the posterior position as in the anterior one. Operative delivery is necessary in about the same proportion of cases. In one respect only is occiput posterior different from occiput anterior. The first stage of labor is one to two hours longer and the second stage longer by a few minutes only.

Further careful observation has not changed these previous conclusions except in one respect. We have recently discovered that occiput posterior does not lead to a longer first stage of labor. In that one respect our previous statement was not correct. We can now say that the only difference between occiput posterior and occiput anterior is that of a few minutes in the duration of the second stage of labor.

In this presentation we shall try to show (1) why the first stage of labor is of the same duration in occiput posterior as in occiput anterior and (2) we shall try to determine the reasons for the difference in duration of the second stage.

FIRST STAGE

In a recent study² of a considerable series of patients seen at the very onset of labor, it has been possible to predict the duration of the first stage on the basis of the relative degree of effacement of the cervix, the consistency of the cervix, the station of the presenting point, and the character of the labor pains. Other factors, previously considered important, were shown to be negligible in importance, and, of these four factors, station is much less important than the other three. It was found that those primiparas entering labor without complete effacement of the cervix had labors about three hours longer than those whose cervixes were effaced when labor began. A relatively firm cervix (of

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

the consistency of the ala of the nose) resulted in labors about three hours longer than those with softer cervices (of the consistency of the lip). Those primiparas who had good pains (a frequency of three minutes or less with at least fair intensity) at the beginning of the dilatation phase would exhibit, under otherwise ideal conditions, a first stage of about three hours. Those whose pains were only fair (of either poor intensity or longer frequency, but not both) would require about six hours to complete their dilatation. Poor pains (of both a weak intensity and long interval) under otherwise favorable conditions needed some twelve hours to bring about dilatation.

These above factors were found to be quite constant in individual patients. Two conditions only affect one's ability to predict the duration of labor on the basis of these findings. Occasionally a patient will enter labor with an uneffaced cervix and will spend long hours in the effacement process to be followed by rather good pains during the dilatation phase. This is unusual. Ordinarily where the pains are very poor and infrequent during the effacement period, they will also be poor and infrequent during the dilatation period. In the second place, one will occasionally observe secondary inertia beginning at 6 or 8 cm. dilatation in a patient whose pains have been previously good and whose progress has been correspondingly rapid. This also is unusual and was observed only three times in the present series of over one thousand patients. Ordinarily, secondary inertia occurs in patients whose pains have previously been poor and whose progress has correspondingly been slow.* If, then, all of the usual variations in labor can be explained on the basis of cervix, station, and labor pains, some explanation becomes necessary for the apparently longer first stage of occiput posterior.

Table I shows the twelve groups (according to cervix and labor pains) with the incidence of occiput anterior and occiput posterior in each group along with the average duration of the first stage of labor in hours and minutes. The consideration of station was omitted as to have included it would have doubled the number of groups and added little to the clearness of the exposition. In 9 of the 12 groups, occiput posterior had a shorter duration of the first stage than occiput anterior. In the remaining 3 groups, occiput posterior showed a longer duration. In several of these groups the number of cases is quite small which, we be-

*Much of our present conception of the possible difficulty to be encountered with occiput posterior has come from careful observation of just the second stage of labor in individual patients where difficulty has arisen. Where similar difficulty has arisen in the second stage in occiput anterior, we have perhaps ascribed that difficulty to its real cause, as occiput posterior was not present and could not be blamed. We have also failed to take cognizance of the fact that the second stage of labor is an entirely different process than the first stage of labor and that the first stage is governed by factors, some of which are not present at all in the second stage. Some of our mis-conceptions of the first stage of labor have arisen from the fact that we do not see our patients until after they have been in labor for some hours and part of the process has already been completed. We cannot then know the status which was present at the beginning of their labors. This recent group of patients were all seen at the very onset of their labors and the conditions present at that time accurately recorded.

TABLE I. PRIMIPARAS, FIRST STAGE

CERVIX	PAINS	OCCIPUT ANTERIOR	OCCIPUT POSTERIOR
Effaced, soft	Good	103 Pt., 3 hr. 57 min.	51 Pt., 3 hr. 41 min.
Effaced, firm	Good	17 Pt., 4 hr. 36 min.	7 Pt., 4 hr. 30 min.
Not effaced, soft	Good	65 Pt., 6 hr. 13 min.	48 Pt., 6 hr. 03 min.
Not effaced, firm	Good	14 Pt., 8 hr. 25 min.	21 Pt., 7 hr. 43 min.
Effaced, soft	Fair	38 Pt., 7 hr. 04 min.	32 Pt., 6 hr. 43 min.
Effaced, firm	Fair	16 Pt., 10 hr. 34 min.	17 Pt., 10 hr. 51 min.
Not effaced, soft	Fair	49 Pt., 8 hr. 00 min.	49 Pt., 10 hr. 19 min.
Not effaced, firm	Fair	15 Pt., 14 hr. 10 min.	20 Pt., 12 hr. 32 min.
Effaced, soft	Poor	17 Pt., 16 hr. 04 min.	23 Pt., 13 hr. 24 min.
Effaced, firm	Poor	7 Pt., 16 hr. 16 min.	9 Pt., 19 hr. 37 min.
Not effaced, soft	Poor	13 Pt., 23 hr. 45 min.	23 Pt., 17 hr. 46 min.
Not effaced, firm	Poor	12 Pt., 25 hr. 15 min.	15 Pt., 21 hr. 59 min.

lieve, accounts for the discrepancy of hours between occiput anterior and occiput posterior, as it is our present belief that occiput posterior does not have a shorter first stage than occiput anterior nor a longer first stage, but an identical first stage under like conditions of effacement, consistency of the cervix, and character of labor pains.* (Absolute accuracy should include a consideration of station also.)

Table II shows the similar data for multiparas. Here we find six groups where the occiput posterior labor averaged slightly longer, four groups where it is less, and one of equal length. The number of patients in this multiparous series is so small as to be inconclusive.

We would like particularly to call attention in Table I to the tendency of occiput posterior to be associated with unfavorable conditions of uneffacement and firm consistency of the cervix and also the relatively greater proportion of occiput posterior patients whose pains are only fair or actually poor. One might debate as to whether occiput posterior tended to result in poor pains, or firm or uneffaced cervix. Such statements have been made by some observers. Potter has, on the other hand, suggested that possibly all labors start as occiput posterior,

TABLE II. MULTIPARAS, FIRST STAGE

CERVIX	PAINS	OCCIPUT ANTERIOR	OCCIPUT POSTERIOR
Effaced, soft	Good	43 Pt., 2 hr. 4 min.	27 Pt., 2 hr. 14 min.
Effaced, firm	Good	5 Pt., 2 hr. 40 min.	1 Pt., 2 hr. 15 min.
Not effaced, soft	Good	44 Pt., 3 hr. 38 min.	35 Pt., 3 hr. 39 min.
Not effaced, firm	Good	10 Pt., 4 hr. 45 min.	8 Pt., 4 hr. 32 min.
Effaced, soft	Fair	18 Pt., 4 hr. 40 min.	17 Pt., 4 hr. 19 min.
Effaced, firm	Fair	3 Pt., 4 hr. 3 min.	1 Pt., 4 hr. 10 min.
Not effaced, soft	Fair	31 Pt., 5 hr. 43 min.	26 Pt., 6 hr. 16 min.
Not effaced, firm	Fair	8 Pt., 8 hr. 43 min.	10 Pt., 8 hr. 01 min.
Effaced, soft	Poor	8 Pt., 5 hr. 25 min.	5 Pt., 6 hr. 00 min.
Effaced, firm	Poor	0 Pt., - hr. - min.	0 Pt., - hr. - min.
Not effaced, soft	Poor	11 Pt., 9 hr. 27 min.	16 Pt., 10 hr. 08 min.
Not effaced, firm	Poor	4 Pt., 11 hr. 23 min.	2 Pt., 16 hr. 40 min.

*A study of attitude is in progress and will be submitted later.

and we might reason that early rotation to an anterior position is the result of a favorable cervix and good labor pains. Whatever one's belief may be, these data show that more than 150 occiput posterior patients, under favorable conditions of cervix and pains, had very short labors, whereas none of the patients with occiput posterior or occiput anterior with unfavorable conditions of cervix and pains had short labors. The 49 patients with occiput anterior with poor pains had an average first stage of twenty hours and twenty-three minutes, and the 70 patients with occiput posterior with poor pains had an average first stage of seventeen hours and twenty-eight minutes. This would suggest that possibly occiput posterior was even more favorable than occiput anterior under these circumstances. We do not believe this to be true; we do believe, however, that occiput anterior and occiput posterior will have a first stage of the same duration under exactly similar conditions of cervix and labor pains.

SECOND STAGE

When one attempts to analyze the various factors involved in the second stage of labor, one encounters certain forces and resistances which do not lend themselves readily to measurement. The voluntary effort of the patient, of course, varies widely, but we have not, as yet, known how to apply any measurement or estimate of the relative value of this voluntary effort in a given patient. It is almost totally lacking in some patients while in others it is of greater import than the involuntary contractions of the uterus. This is particularly true in multiparas, but is also observed infrequently in primiparas. The resistance offered by the pelvic floor and vulva is also rather difficult to measure. In a previous publication,³ we pointed out that large babies resulted in a longer average second stage than was necessary for the medium and smaller sizes. This factor was negligible in multiparas but was a definite quantity for primiparas.

In the present comparison of occiput posterior and occiput anterior, only two other variables were analyzed: first, the labor pains; and, second, the time of internal rotation. Labor pains were said to be good (for purposes of this study) when they were of strong intensity or were of fair intensity and not more than two minutes apart. They were said to be poor if they were of very weak intensity or if they were of fair intensity but at an interval greater than two minutes.

Inasmuch as one of the principal differences between occiput posterior and occiput anterior is in the degree of internal rotation necessary, we made it a point to study internal rotation in some detail, noting when it occurred with respect to both the first and second stages of labor and also when it occurred relative to station in the pelvis. In a previous publication, we had already pointed out that the percentage of spon-

taneous internal rotation in occiput posterior was the same as for occiput anterior. We also indicated that more than one-third of either group did not exhibit internal rotation until after the pelvic floor had been reached. In the analysis which follows, the term "rotated" is applied to those patients where internal rotation takes place before or at the moment that the presenting point reaches the pelvic floor. "Unrotated" is applied to those cases where rotation takes place on the pelvic floor or delivery occurs without internal rotation.

The presenting point reaches the pelvic floor before or at about the same time as dilatation is completed in about one-half of all patients. There is no "descent" phase of the second stage in these patients. In the remaining half, the head may be at a variable distance above the pelvic floor at the time of completion of dilatation, and anywhere from a few minutes up to one-half hour or more may elapse before the presenting point reaches the pelvic floor. In these patients the same "pelvic floor" phase must then ensue. Obviously this second group of patients will have a second stage considerably longer in comparison than the other group and, therefore, cannot be compared directly. We have chosen, therefore, to divide the second stage into the two phases of "descent" and "pelvic floor" in this comparison of occiput posterior and occiput anterior. Table III for primiparas and Table IV for multiparas will present the data according to this plan. (These are the spontaneous deliveries; operative deliveries are treated in Table V.)

TABLE III. PRIMIPARAS, SECOND STAGE

	PAINS		OCCIPUT ANTERIOR	OCCIPUT POSTERIOR
Descent	Good	Rotated	211 Pt., 12.9 min.	170 Pt., 13.9 min.
	Good	Unrotated	104 Pt., 11.8 min.	84 Pt., 13.8 min.
	Poor	Rotated	79 Pt., 25.6 min.	54 Pt., 27.4 min.
	Poor	Unrotated	56 Pt., 21.5 min.	48 Pt., 34.8 min.
Pelvic floor	Good	Rotated	380 Pt., 33.3 min.	304 Pt., 37.6 min.
	Good	Unrotated	213 Pt., 37.9 min.	158 Pt., 49.2 min.
	Poor	Rotated	118 Pt., 55.0 min.	98 Pt., 60.8 min.
	Poor	Unrotated	96 Pt., 60.5 min.	78 Pt., 81.5 min.

TABLE IV. MULTIPARAS, SECOND STAGE

	PAINS		OCCIPUT ANTERIOR	OCCIPUT POSTERIOR
Descent	Good	Rotated	156 Pt., 7.2 min.	96 Pt., 7.6 min.
	Good	Unrotated	67 Pt., 5.8 min.	55 Pt., 9.7 min.
	Poor	Rotated	37 Pt., 14.1 min.	37 Pt., 16.2 min.
	Poor	Unrotated	30 Pt., 13.5 min.	30 Pt., 17.8 min.
Pelvic floor	Good	Rotated	310 Pt., 11.5 min.	198 Pt., 12.8 min.
	Good	Unrotated	133 Pt., 12.4 min.	111 Pt., 15.2 min.
	Poor	Rotated	69 Pt., 20.2 min.	55 Pt., 16.5 min.
	Poor	Unrotated	59 Pt., 23.2 min.	52 Pt., 30.0 min.

THE DESCENT PHASE

The descent phase of the second stage in occiput posterior is not strikingly different from in occiput anterior. Where rotation occurs during descent (about two-thirds of all patients), the difference in time between occiput posterior and occiput anterior is not over one or two minutes. On the other hand, where descent occurs without internal rotation, the difference may be more marked. If the pains are good, the differential is apparently a matter of two or three minutes only. In the presence of poor pains, the difference in multiparas is about four minutes. In primiparas, whose pains were poor, there were:

	OCCIPUT ANTERIOR	OCCIPUT POSTERIOR
Medium-sized babies	45 Pt., 23.7 min.	34 Pt., 29.6 min.
Large babies (over 3,500 Gm.)	16 Pt., 22.0 min.	15 Pt., 42.7 min.

The number of patients observed in each of these groups is so small that no definite conclusion should be drawn. It seems unlikely, however, that as much as twenty minutes' difference exists between occiput anterior and occiput posterior even under the unfavorable conditions of poor pains, large babies, and lack of internal rotation.

There were altogether eight instances of failure of descent, 2 occiput anterior and 6 occiput posterior. In only one instance were the pains of even fair intensity and frequency. In three instances the pains were so weak and so far apart that labor could almost be said to have ceased altogether. In only two instances was the baby very large (3,885 Gm.; 4,035 Gm.). Moderate deflexion of the head was present in two cases. The occiput posterior position was thought to have contributed to the failure of descent in two or possibly three of these cases.*

THE PELVIC FLOOR STAGE

In the pelvic floor or expulsion phase, one notes a consistently present difference between occiput anterior and occiput posterior. Even in the presence of good pains with the head completely rotated occiput posterior will require from three to six minutes more in the expulsion phase. Oddly enough the same difference was observed when the pains were poor: One would expect that the completely rotated occiput posteriors might be exactly like completely rotated anteriors. That such is not the case can possibly be explained by imperfect dispersion of the expulsive forces on the markedly rotated head. When rotation occurs after the head reaches the pelvic floor or fails to occur, those patients delivered

*One of these six posterior cases had completely rotated and was delivered after sixty-one minutes of second stage pains by median forceps. The baby weighed 4,035 Gm. In another, manual rotation and median forceps after 290 minutes (thought to be due to injudicious use of twilight sleep) delivered a baby weighing 3,300 Gm. No. 3. Median forceps rotation and delivery after seventy-four minutes (3,150 Gm.). No. 4. Median forceps rotation and delivery after 130 minutes (3,885 Gm.). No. 5. Median forceps delivery without rotation, 100 minutes (3,870 Gm.). No. 6. Median forceps delivery without rotation after seventy-five minutes (3,110 Gm.). The two occiput anteriors were delivered by median forceps rotation and extraction, one after eighty-three minutes (3,430 Gm.) and one after 155 minutes (2,770 Gm.).

spontaneously will show an average difference of eight to twelve minutes if the pains are good and fourteen to seventeen minutes when the pains are poor. The longer arc of internal rotation would seem to be a partial explanation for this time difference.

Failure of internal rotation in the time allotted (the length of time varied according to our clinical judgment in the individual patient) was observed nineteen times in the occiput anterior primiparas (2 per cent). The importance of this datum was not recognized early in the study, and we probably failed to observe several additional instances in the occiput anterior cases. Failure of rotation in the occiput posterior primiparas was observed forty-six times (5.9 per cent). In exactly half of these patients (23), spontaneous delivery took place with the occiput posterior and with an average pelvic floor phase of sixty-six minutes. Five of the persistent occiput anteriors also delivered spontaneously without rotation. This left a remainder of 14 unrotated occiput anteriors and 23 unrotated occiput posteriors to be delivered by operative procedure. This intervention was thought necessary after an average of one hundred minutes for the occiput anteriors and one hundred twenty-five minutes for the occiput posteriors. Whether the failure of these two groups of 14 and 23 patients to deliver spontaneously in the time allotted should be ascribed to poor labor pains, or to failure of rotation, or to oversized baby, or to moderate degrees of extension of the head, or to all of these causes combined, we cannot yet say as the number of patients available for study is far too small from which to draw exact conclusions. The only positive statement is that an increased operative incidence of nine (or ten) in a series of 780 occiput posterior primiparas was observed in this series.

That operative delivery was not otherwise more frequent for occiput posterior than for occiput anterior is well shown in Table V.

TABLE V. PRIMIPARAS, OPERATIVE DELIVERY

	OCCIPUT ANTERIOR	OCCIPUT POSTERIOR
<i>Good Pains</i>		
Maternal and fetal distress	13 Pt., 21.2 min.	13 Pt., 33.5 min.
Lack of progress { Rotated	28 Pt., 60.3 min.	19 Pt., 65.3 min.
Unrotated	3 Pt., 106.0 min.	2 Pt., 98.5 min.
<i>Poor Pains</i>		
Maternal and fetal distress	13 Pt., 39.6 min.	10 Pt., 26.4 min.
Lack of progress { Rotated	62 Pt., 99.4 min.	63 Pt., 93.6 min.
Unrotated	11 Pt., 98.1 min.	21 Pt., 127.3 min.
Total patients in series	955	780

In summary then, the second stage in occiput posterior can be said to be as much as thirty-five minutes longer for occiput posterior, depending upon the associated factors of labor pains, infant size, station at which dilatation is completed, and the time at which internal rotation

takes place; operative intervention was, in our judgment, necessary in this series in 1 per cent more instances than was thought necessary for occiput anterior.

CONCLUSIONS

1. The first stage of labor is dependent upon the condition of the cervix and the character of the labor pains, and is not different for occiput posterior from that for occiput anterior.

2. The second stage of labor in occiput posterior presents more work to the expulsive forces in order to rotate the head through the necessarily greater arc as represented by a time difference of two to thirty-five minutes in primiparas. Part of this time difference may, however, be the result of the (greater arc of rotation of the head on the body and consequent) misdirection of expulsive force.

3. Our clinical judgment dictated the use of low forceps in (unrotated) occiput posterior more frequently than in occiput anterior; 10 additional instances in 780 occiput posteriors.

REFERENCES

1. Calkins, L. A.: *AM. J. OBST. & GYNEC.* **38**: 993, 1939.
2. Calkins, L. A.: *AM. J. OBST. & GYNEC.* **42**: 802, 1941.
3. Calkins, L. A., Litzenberg, J. C., and Plass, E. D.: *AM. J. OBST. & GYNEC.* **22**: 604, 1931.

DISCUSSION

DR. R. T. LAVAKE, MINNEAPOLIS, MINN.—Experience, I believe, shows that, given equal degrees of deflexion, the length and difficulties of labor would vary in the first stage according to the character of the pains, the condition of the cervix, and to some extent to the station of the head; in the second stage according to the character of the pains, the station of the head, and the need of rotation.

Realizing that accurate measurements of degrees of deflexion, even if possible, would complicate his investigation tremendously, Dr. Calkins has relied upon a fortuitous averaging of this factor of deflexion. He has limited himself to factors that lend themselves to more accurate mensuration and tabulation.

Experience has, however, taught that under equal conditions of cervix and uterine contractions, the length of labor will vary directly with the degrees of deflexion present. If one is inclined to question this generalization, let him compare the length of labor of a few frontocotyloid attitudes or a few brow presentations, with a like number of well-flexed heads in either anterior or posterior positions.

Now the figures in Dr. Calkins' paper demonstrate that, with the same conditions of the cervix and of pains, the length of labor was approximately the same in the two groups of anterior and posterior positions. This equality in length of labor can only be interpreted as showing that in these samples, the average degrees of deflexion happened to be approximately the same. Had the average of deflexion been unequal, the average length of labors would not have been equal.

It is not surprising that Dr. Calkins' previous report, that he mentions, and the present report differ as to the lengths of labor. These differences are merely due to the differences in the averages in these two samples, of the hidden factor, deflexion. If we did not know accurately the comparative amounts of deflexion, we would not be in a position to argue that posterior positions are no more to be feared than anterior positions. To so argue would be to commit what is known in logic as the fallacy of neglected aspect.

It is interesting that they show a tendency for greater length of labor in the posterior positions, because this would tend to confirm the opinion held by most of us, I believe, that in both theory and practice the potential for deflexion is greater in posterior than in anterior positions.

DR. J. BAY JACOBS, WASHINGTON, D. C.—In the vast majority of cases, as demonstrated by roentgenography, the head has a tendency to engage with the biparietal diameter in the true conjugate. The character of the pelvic floor, type of labor pains, pelvis and so on, will determine whether the occiput will rotate anteriorly or posteriorly.

Certain authors (as Danforth) state that 70 per cent of primary occipitoposteriors will rotate anteriorly, while certain others think that 90 per cent will rotate. That more than 90 per cent can rotate anteriorly has been shown by Dr. Calkins, who appears to be very conservative. Of course, the men who claim that only 70 per cent will rotate anteriorly generally interfere earlier. At times it does pay to interfere in an occiput posterior, because I, personally, feel that labor, particularly in the persistent type, takes much longer than in the anterior variety.

A prolongation of only twenty minutes of the second stage in the group where circumstances were shown to be unfavorable, may be misinterpreted. It would take only two or three persistent posteriors to make that much difference in a large series of cases.

Dr. Calkins has been very fortunate in his series of cases to have had only three in 1,000 in which we may say that progress of labor stopped after the cervix was only a few centimeters dilated. Persistent occiput posterior offers me a lot more concern than seems to be the present general attitude.

DR. SAMUEL A. COSGROVE, JERSEY CITY, N. J.—I would like to ask Dr. Calkins if any of these cases had been subjected to analgesia during the first and second stages. His average time for the whole succession of events, which he recognizes in his report, seems very short as compared with my own experience. I wonder if part of the difference is due to the fact that analgesia has been entirely eliminated in his study of the mechanism of labor?

DR. B. H. CARROLL, TOLEDO, OHIO.—Were the patients all kept in bed, or were some of them allowed to get up and move around? If the latter, were abdominal binders or something of that sort used?

DR. CALKINS (closing).—We are conducting a similar study on the question of deflexion, but we do not yet have definite conclusions. I had in the beginning exactly the same impression as Dr. LaVake concerning the deflexion attitudes. I have not yet been convinced that that impression is wrong, but I think that perhaps deflexion represents a state of unpreparedness for labor, just as occiput posterior may represent a state of unpreparedness for labor. A deflexion attitude would perhaps not exist except for the fact that the lower uterine segment is not stretched out, the cervix is not effaced, and the state of tonicity is not satisfactory. I think it may be the result rather than the cause.

There is something more than just coincident equality of deflexion between the occiput anteriors and occiput posteriors in this series. Perhaps I did not clearly point out that in the previous series where we did recognize a difference in time between occiput posterior and occiput anterior, we did not realize the more frequent association of firm cervixes and poor labor pains with occiput posterior. This time we have recognized that association and we have therefore completely altered our previous conception that posterior occiput does make for a long labor. I would like to repeat that under like conditions of cervix and labor pains the length and ease of the first stage of labor are exactly the same for posteriors and anteriors.

We recognize as the end of the first stage of labor the time when the cervix can no longer be felt by rectal or vaginal examination. We had only four or five instances in this whole series, where the second stage was as much as two and one-half hours long.

Misconception about the second stage of labor has been due in part to the fact that men have regarded the first stage as ended when they decided that the cervix was sufficiently dilated to let the head come through. We insist on waiting until the cervix cannot be felt. The minute the cervix ceases to be the determining influence there is much more rapid progress. Our second stage is shorter because we determine the beginning of the second stage differently.

Our patients have plenty of analgesia, sometimes a little too much. As for the first-stage analgesia, in my private patients, I start giving nitrous oxide in analgesic doses as soon as the pains become at all hard. We do not use any other analgesic except morphine, when it seems to be indicated. I cannot say what proportion of patients receive morphine. It is given on indication.

TRANSVERSE PLICATION OF THE RECTUM FOR THE REDUCTION OF LARGE RECTOCELES*

WALTER T. DANNREUTHER, M.D., F.A.C.S., NEW YORK, N. Y.

(From the Department of Gynecology, New York Post-Graduate Medical School and Hospital, Columbia University)

A POSTOPERATIVE protrusion through the vulvar orifice after a vaginal operation is a disappointment to the patient and embarrassing to the operator. Inversion of the vagina after hysterectomy, recurrence of prolapse after an interposition or Manchester operation or a colpectomy, and the reappearance of a cystocele after colporrhaphy, can usually be attributed to faulty surgical technique. Persistent distention of the posterior vaginal wall, following various plastic procedures, is sometimes due to the presence of an overlooked enterocele in the cul-de-sac which should have been corrected. On the other hand, there are some cases of lacerated perineum associated with a large rectocele, for the cure of which a perineorrhaphy alone is entirely inadequate, despite the absence of a true posterior vaginal hernia. The chief anatomic defect in a perineum damaged by birth trauma lies in the impairment of its muscular integrity, particularly a diastasis of the vaginal fibers of the levator ani, and a satisfactory surgical repair depends upon the proper restoration of the perineal body, regardless of the mucous membrane incisional design. When, however, there is a coexisting large and high rectocele, it is equally as necessary to dispose of the redundancy in the rectal wall as to repair the damage sustained by the perineal musculature. Otherwise, the bulging rectum may again

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

overstretch the mucosa of the posterior vaginal wall and present itself at the vaginal orifice. The reduction in size of the dilated rectum is usually accomplished by plicating the anterior wall on its longitudinal axis, and then reinforcing the first suture line by a superimposed approximation of the pararectal tissues. This method really fails to take up the slack in the atonic longitudinal muscle fibers in the rectal wall and incidentally narrows its lumen. It, therefore, seems much more logical to infold the rectal wall on its transverse axis, thus affording the muscle fibers an opportunity to regain their lost tonicity, and preserving the normal caliber of the rectal canal. For many years I have

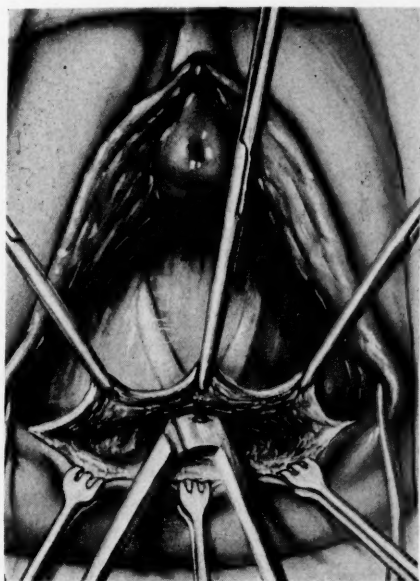


Fig. 1.

Fig. 1.—Transverse incision and separation of the vaginal and rectal walls.

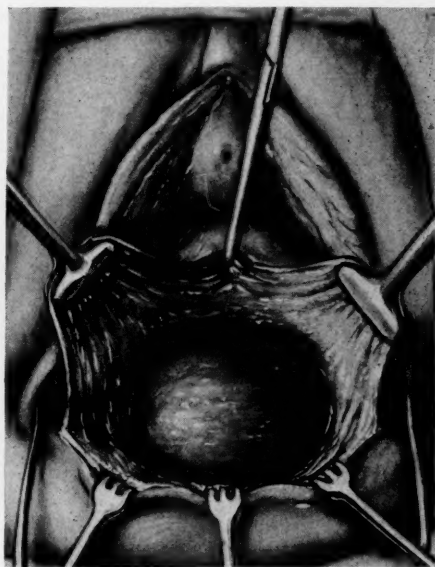


Fig. 2.

Fig. 2.—Free mobilization of the rectocele.

utilized such a procedure with gratifying results, and venture to describe it in detail without any pretense of originality. I can only say that I have not read a description of the technical steps elsewhere or seen any other operator in this country or abroad dispose of a rectocele in the same way.

METHOD

The fourchette is incised transversely and the lower margin of the wound grasped with three tenaculum clamps. At the same time, an assistant applies three Ochsner clamps at opposite points on the edge of the vaginal mucous membrane. A curved Mayo scissors is then thrust between the posterior vaginal wall and the anterior rectal wall to the apex of the rectocele (Fig. 1). By widely separating the blades of the scissors, the vagina and rectum are easily and bloodlessly detached

from each other. After removing the Ochsner clamps, the vaginal mucous membrane is cut in the midline with straight scissors to the upper limit of the rectocele. The angle of the incision is elevated with an Ochsner clamp and the margins of the two mucous membrane flaps

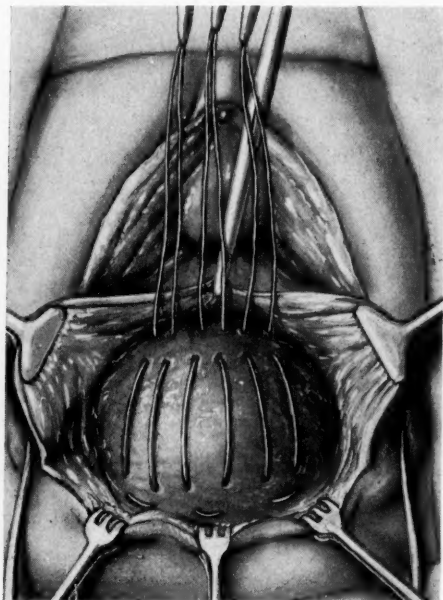


Fig. 3.—Placing the three Pagenstecher linen sutures.

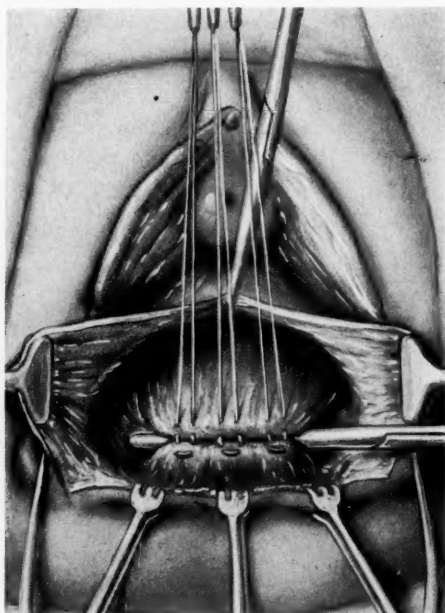


Fig. 4.—Infolding the rectal wall after pulling the mattress sutures taut.

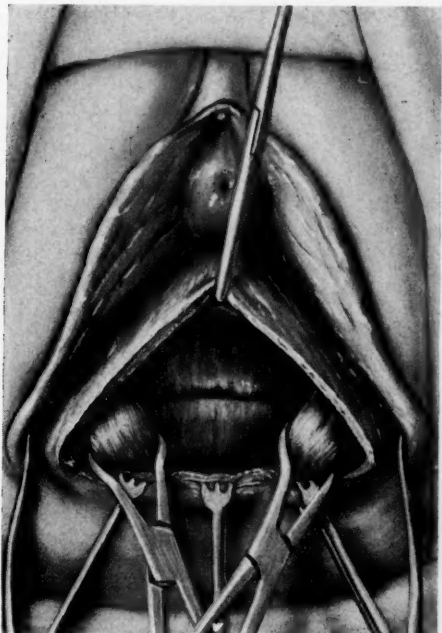


Fig. 5.—Elevation of the vaginal fibers of the levator ani with their overlying fascia.



Fig. 6.

Fig. 6.—Approximation of the levator ani muscles with two encircling kangaroo sutures.

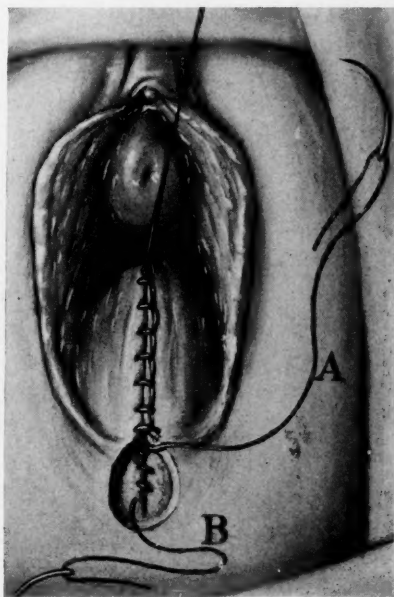


Fig. 7.

Fig. 7.—The interlocking chromic catgut suture (A) is laid aside while the perineal fascia is closed with a running chromic suture (B), and then used again to close the perineal skin with a few subcuticular bites.

with T clamps (Fig. 2). The bulging rectum is then freely mobilized laterally by means of gauze covered finger dissection, and the separated vaginal fibers of the levator ani muscle with their overlying fascia exposed in the same way. After fastening the handles of the T-clamps to the patient's buttocks on each side with towel clamps, three Pagenstecher linen mattress sutures are placed in the rectal wall from above downward, leaving them quite loose and holding their long ends temporarily with clamps (Fig. 3). An assistant inserts a hemostat or other straight instrument transversely beneath the slack sutures, and infolds the rectal wall evenly before the three sutures are pulled taut simultaneously (Fig. 4). As the first one is tied, the assistant slips the tip of the hemostat from underneath it, again from under the one in the midline, and finally withdraws it completely as the third one is knotted. The excess of vaginal mucous membrane on each side is then cut away, leaving a triangular area to be closed. The rectum is guarded by a finger as the assistant makes traction on one of the lateral tenaculum clamps to expose the fascia covering the levator ani fibers on that side. These structures are picked up in a towel clamp, and the same steps are carried out on the opposite side (Fig. 5). The separated muscle fibers are then encircled with two or more medium-sized kangaroo tendon sutures which are tied sufficiently tight so that the muscles are approximated in the midline without strangulation (Fig. 6). Before the ends are cut, the vaginal orifice is tested to see that it will comfortably accept the introduction of two fingers. The margins of the vaginal flaps are brought together with an interlocking continuous chromic catgut suture, which starts at the upper angle, picks up the rectal wall in its first bite, and is continued down to the fourchette. This suture is then laid aside, while the perineal fascia is closed with another chromic running suture (Fig. 7), after which it is used again to close the perineal skin with a few subcuticular bites. A strip of iodoform gauze is placed in the vagina, and a dry vulvar pad applied. The gauze is removed after forty-eight hours and the perineum kept dusted continuously with thymol iodide. No douches are allowed. An enema is given on the third day, and bowel movements permitted thereafter.

I have done this operation with uniformly satisfactory end results, except in one case in which I carelessly neglected to include the rectal wall in the first bite of the suture starting at the upper angle of the vaginal wound. This patient developed a small prolapse of the rectum through the anus, which was easily reduced. Incidentally, these technical steps seem to contribute materially to the early restoration of bowel function.

580 PARK AVENUE

DISCUSSION

DR. LOUIS E. PHANEUF, BOSTON, MASS.—It is admitted that a myorrhaphy of the levators or an ordinary reconstruction of the perineum will not overcome a large rectocele. Longitudinal plication of the rectum may work satisfactorily in the lesser degrees of rectocele, but very unsatisfactorily in the large rectoceles.

In July of this year I had occasion to use this procedure for the first time in an extremely large rectocele. In this case I first opened the cul-de-sac of Douglas

to rule out an enterocele. The rectocele itself was of such size that I had to plicate the rectum in three layers, but the result was highly satisfactory.

DR. EMIL NOVAK, BALTIMORE, MD.—The procedure advocated is certainly much more conservative than one suggested many years ago of actually resecting the redundant portion of the rectum in cases of very large rectocele. On the other hand, I feel that even Dr. Dannreuther's procedure should rarely be necessary, because of the strong tendency of the redundant bowel to involute and regain its normal caliber once the rectocele has been properly corrected.

Both Dr. Dannreuther and Dr. Phaneuf have emphasized the futility of the ordinary outlet repair, with simple approximation of the levator muscles, in the correction of the large rectocele which often involves the entire rectovaginal septum, representing a hernia of the rectum through the latter. When simple perineorrhaphy is done in such cases, the patient is quite sure to return with the large rectocele bulging into or out of the vagina over the margin of the united levators. The rectovaginal septum, however, can be satisfactorily and easily restored by one of various techniques, depending partly on individual indications and partly on the preference of the operator.

A useful technique, which I frequently employ, is that suggested many years ago by Dr. George G. Ward and Dr. Albert Spalding, quite independently. By this method the rectum is elevated and rotated on its transverse axis upward toward the pelvis, accomplishing essentially the same result as Dr. Dannreuther's procedure. In other cases the septum can be restored by transverse approximation of the vaginal fascia which is continuous with the levator fascia. Whenever possible we should avoid techniques which involve placing sutures through the rectal wall itself, because of the theoretical possibility of an occasional rectovaginal fistula. This was a fault of the original Ward-Spalding technique which subsequent modification has eliminated.

DR. JAMES W. KENNEDY, PHILADELPHIA, PA.—I have stated a number of times that repair of the perineum was a lost art and that over 60 per cent of the repairs of the perineum which we perform have had one or more previous attempts at repair, ending in failures.

In these large rectoceles the prerectal tissues bulge forward, producing an extensive hernia in the posterior vaginal wall. The muscular and fascial planes, upon which the stability in the repair of the perineum depends, have been so widely separated that it becomes necessary to reduce the hernia of the prerectal structures before the muscular and fascial tissues can be properly approximated. This, Dr. Dannreuther has done by his transverse plication of the prerectal tissues. I always reduce the large protruding mass by plication of the tissues with the use of fine silk sutures. I finish the repair of the perineum by interrupted mass sutures of silkworm-gut.

In many of these extensive posterior lacerations, I feel that failure occurs on account of the too early absorption of the suture material which has been used. After seventy-two hours much of the tensile strength of any absorbable material is lost, and as there is abnormal tension placed on the sutures following the repair of these extensive vaginal hernias, too often muscular and fascial retraction will take place before stable union occurs.

DR. A. D. CAMPBELL, MONTREAL, CANADA.—The principle in the repair of a large rectocele lies not only in the reconstruction of the perineum but in reconstructing the rectovaginal septum throughout its entire length. I can readily see how a form of intussusception might follow such an operation if not properly done, and for this reason I am rather doubtful as to the general employment of transverse

plication. I have always felt that a colossal rectocele is but the visible portion of an existing megacolon. The operation of plication as advised by Dr. Dannreuther appeals to me in the surgical treatment of those cases where the rectocele has reached tremendous proportions.

DR. DANNREUTHER (closing).—This operation is indicated only in cases of large rectoceles. After many years of experience with this procedure, I have never seen a subsequent rectovaginal fistula. Should one occur, it would be due to faulty technique.

MIDLINE EPISIOTOMY*

J. P. PRATT, M.D., C. P. HODGKINSON, M.D., AND C. R. KENNEDY, M.D.,
DETROIT, MICH.

(From the Division of Gynecology and Obstetrics, Henry Ford Hospital)

THE claim that midline episiotomy is more comfortable than medio-lateral constitutes a challenge. The impression is so prevalent that several texts express preference for the midlocation if satisfactory healing can be assured. It has been our experience that the midline is safer and more satisfactory than the other approach.

Strict adherence to all surgical principles is important in obstetrics. The employment of aseptic technique is indispensable. Sharp dissection of tissues, complete hemostasis, and careful apposition of tissues by non-constricting sutures remain pertinent points. Improvement in methods and the adoption of new ideas and materials to replace less valuable procedures mark the progress of the times. The fields of preoperative sedation and anesthesia are notable examples. Stay sutures embracing large volumes of tissue are gradually being discarded, and the trend is now toward the use of finer suture material.

Division of perineal structures by a sharp scalpel offers less tissue insult than the crushing effect of scissors. Contusion of tissues by blunt instruments is a source of pain. Such devitalized tissue margins offer a nidus for infection. Edema and swelling are natural companions. Less perineal scarring and more rapid healing are additional merits of sharp dissection.

Mass ligation of tissue with through-and-through sutures favors pocket formation with retention of old blood. This is particularly important because the perineum is a contaminated field and care must be taken to obliterate all dead spaces. Accurate anatomic apposition of tissues promotes the healing process and discourages the onset of infection.

The perfect suture material has never been developed. It has long been recognized that buried catgut is a tissue irritant, and for some

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

time it has been suspected that it is a factor in the dehiscence of episiotomy wounds. Suture material is constantly being improved. The recent standardization by the United States Pharmacopoeia is an important step in the right direction. For the first time this gives us an opportunity to compare accurately the results obtained by different observers. Adoption of the United States Pharmacopoeia standards by all manufacturers will facilitate further comparison.

We believe that adherence to each one of these surgical principles is fundamentally important in perineal surgery. Numerous authors have emphasized one or more of these points. The earliest writers on episiotomy advocated a knife-edge for making the episiotomy wound.

Rucker¹ has pointed out in a detailed history of episiotomy that the blunt-pointed bistoury was one of the first instruments used. Pieri² and Gillis³ have recently stressed to the obstetrician the importance of anatomic knowledge of perineal structures. Pieri,² Royston⁴ and others have called our attention to the use of fine catgut. Phaneuf⁵ has pointed out the importance of layer suturing. The edema and swelling of the perineum following episiotomy and repair are recognized by all as a source of discomfort. To accommodate for this edema a method using a continuous knotless suture for reconstructing the perineum has been outlined recently by Rucker.¹

We are in accord with the various procedures just cited but wish to emphasize the importance of using them all.

For several years we have been using smaller and smaller catgut with increasing satisfaction, and for the past three years we have used five-0 chromic catgut for repair of episiotomy wounds. All incisions are made with a scalpel. Small bites of tissue with complete hemostasis and accurate anatomic apposition of tissue is practiced. We wish to stress that we are presenting nothing new, but feel that the suture material, recently made available, efficiently adapts itself to improved obstetric care. A simple method is presented which, we believe, offers both objective and subjective improvement.

METHOD

The perineum is allowed to bulge before the episiotomy is elected. We prefer to wait for this stage for two reasons: First, an episiotomy may not be necessary; and second, the pressure of the presenting part thins the perineum and demarcates the structures. A sterile wooden tongue depressor is then slipped into the vagina between the presenting part and the perineum. Pressure is maintained on the fundus to keep the perineum bulging. With a sharp scalpel the incision is begun at the level of the transverse muscle bundle. The incision is continued through all the structures until the scalpel meets the tongue depressor. Care is taken to sever the vulvar ring and the fascia over the anterior and posterior surfaces of the transverse perineal and sphincter muscles.

The episiotomy is repaired after completion of the third stage. Small, round-pointed needles threaded with five-0 chromic catgut are used. The fascia layers are identified and brought together with interrupted sutures embracing small bites of tissue. Particular attention is given to the fascia over the transverse muscle bundle. Care is taken to preserve the triangular shape of the perineum. Complete hemostasis and obliteration of dead spaces are practiced. The vaginal mucosa and skin are closed with interrupted buried sutures.

The aftercare consists of drying the perineum with a sterile towel and protecting it with a sterile pad. A pitcher douche is given after defecation or voiding. If the bowels have not moved by the third day, an enema is given.

DISCUSSION

The efficiency of midline incisions was pointed out in 1918 by Pomeroy.⁶ That this site is the natural cleavage plane is stressed by the frequency of spontaneous lacerations in this location. Permanent injury to muscle fibers can be prevented by a well-timed midline episiotomy. The objection to midline episiotomy is the risk of extension into a third-degree laceration. The misfortunes of this complication have been greatly exaggerated. Pomeroy,⁶ Royston⁴ and others have already shown that a third-degree laceration of the perineum, when properly repaired, heals as readily as if the muscle were not torn. We share this opinion. Since using five-0 chromic catgut for repair, we have had ten cases of third-degree extension of midline incisions. There was no morbidity in any case and extended hospitalization was not necessary. Subsequent examination has shown adequate sphincter control with a well-supported perineum.

The use of the wooden tongue depressor for protection of the presenting part is simple and efficient. The resistance necessary for making the incision with adequate protection to the baby is well provided. Pressure from within aids in demarcating the structures to be incised.

A scalpel is used to incise the perineal body. Directing the knife-edge accurately in the midline insures cutting the fascia in the natural plane of cleavage. The additional space made available by incising the fascia of the transverse muscle bundle is considerable. The pressure of the presenting part forces the fascia edges laterally while the muscle stretches without tearing. The clean-cut edges facilitate closure. Because of the delicate caliber of the suture material, numerous sutures can be placed in a given area without fear of overcrowding with foreign material. The use of small needles (Murphy intestinal No. 4) encourages little additional trauma. Less pain results from the use of submucosal and subcutaneous sutures and permits early sealing of the incision, preventing contamination and reducing the pain. Bower, Burns and Mengle⁷ recently published their results with five-0 chromic catgut for gastrointestinal surgery. The reduction in tissue edema, ecchymosis, and local sloughing with

marked improvement in healing was well demonstrated. This corresponds to our findings over the past few years.

Over 300 patients treated by this method are available for study. The most notable improvement has been in the reduction of perineal pain following delivery. We attempted to obtain as reliable data as possible concerning perineal discomfort. However, subjective responses of patients do not lend themselves well to scientific analysis. We found only an occasional patient who experienced sufficient pain to require treatment. This discomfort was readily relieved by light therapy. All cases healed promptly. No morbidity attributable to episiotomy was evident. Post-partum examination has yielded gratifying results. The decrease in scar formation has been notable. Good perineal reconstruction has been the rule.

REFERENCES

1. Rucker, M. Pierce: *West Virginia M. J.* 33: 145, 1937.
2. Pieri, R. J.: *J. A. M. A.* 110: 1738, 1938.
3. Gillis, R. A. D.: *Am. J. Surg.* 9: 520, 1930.
4. Royston, G. D.: *AM. J. OBST. & GYNEC.* 19: 185, 1930.
5. Phaneuf, Louis E.: *AM. J. OBST. & GYNEC.* 36: 899, 1938.
6. Pomeroy, Ralph H.: *Am. J. Obst.* 78: 211, 1918.
7. Bower, John O., Burns, John C., and Mengle, Harold A.: *Am. J. Surg.* 47: 20, 1940.

DISCUSSION

DR. M. PIERCE RUCKER, RICHMOND, VA.—As much as I dislike the word routine, I do an episiotomy almost routinely in premature deliveries. I do it here for the baby's sake and in the full-term delivery for the mother's sake.

I have not used a knife and the wooden tongue depressor but am inclined to think that it is better than even a sharp pair of scissors. I have reduced the size of the catgut used to "0" and am glad to learn that smaller catgut is satisfactory. I use a continuous suture without knots as that is the only way I have been able to secure accurate apposition without constriction of the tissues when swelling and edema set in.

The only serious disagreement I have with the authors is the site of the incision. I like to keep away from the perianal skin as far as possible. Not only is it surgically dirty, but it is thin and hard to suture satisfactorily. The mediolateral incision gives more room, which is especially helpful when the patient has a funnel or male type pelvis. The disadvantages of the mediolateral episiotomy are more bleeding and possibly an asymmetrical closure. To overcome the bleeding I infiltrate the tissues with novocain and adrenalin. This has the advantage not only of making the procedure less bloody, but it permits one to stop the anesthetic when the head begins to crown. With this plan the babies are wider awake and the uterus has more tone during the third stage. No further anesthesia is needed for the repair. Asymmetry in repair is avoided by accurate anatomic apposition of tissues, and by observing such landmarks as the remains of the hymen, the mucocutaneous junctions and the pigmented skin.

DR. G. D. ROYSTON, ST. LOUIS, MO.—Midline episiotomy has the advantages of being easier to repair, giving a better anatomic result, and causing decidedly less discomfort. Yet I cannot view with equanimity the harmlessness of the third-degree tear. Among my first five midline episiotomies, two multiparas who delivered spontaneously suffered third-degree tears.

The midline incision has therefore certain limitations. These limitations are as follows: 1, any apparent disproportion, including a postmature baby or a child which seems to be unusually large; 2, faulty presentations; 3, contracted pelvic outlet where the narrow pubic arch forces the head backward, so that it must be accommodated at the expense of the posterior segment of the pelvic floor; 4, a low perineum, where the distance between the anus and vagina measures less than two inches. Since following these suggestions no third-degree tears have followed midline incisions in my hands.

DR. HODGKINSON (closing).—In looking over some 46 cases of third-degree laceration of the perineum that have occurred in the Henry Ford Hospital during the past several years, it was discovered that the biischial diameter was in the neighborhood of 9 cm. for most cases. This indicates that a contracted outlet is an important factor in the etiology of this laceration.

THE TREATMENT OF GONORRHEA IN THE FEMALE WITH SULFATHIAZOLE*

DUDLEY R. SMITH, M.D., AND ROGERS DEAKIN, M.D., ST. LOUIS, MO.

(From the Washington University Clinics, St. Louis, Missouri, in cooperation with the State Board of Health of Missouri)

THE recent improvement of results in the treatment of gonorrhea in women at Washington University Clinics is due to five factors:

1. The use of a safe and efficient chemical compound, sulfathiazole.
2. The use of improved methods of culturing the gonococcus on artificial media.
3. The development of improved technique in case finding and case holding.
4. The use of an adequate record form suitable for statistical analysis.
5. The education of the public about gonorrhea and its cure.

In a preliminary report,† we described our own examination and treatment record form for the individual patient. Since that time we have used and found satisfactory the record form recommended by the United States Public Health Service. A work or progress chart of the entire series of cases by weeks is desirable (Fig. 1). Examination of these charts reveals the progress of the individual patient and the clinic as a whole.

The experiences of one of us (R. D.) in the treatment of male gonorrhea since the introduction of the sulfonamides was the determining factor in our selection of sulfathiazole as the nearest ideal compound in eradicating the gonococcus in women. We have not regretted our selection of this drug.

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

†J. Mich. State Med. Soc. 40: 440, 1941.

The newer methods of culturing the gonococcus in the laboratory are more efficient and simplified. The routine use of a culture from the cervix and the urethra will confirm the clinical diagnosis of gonorrhea; it will reveal the carrier and the occasional cases that are not diagnosed clinically. Adequate laboratory facilities were available to us for systematic bacteriologic study through the department of bacteriology of the Washington University Medical School.

TREATMENT OF GONORRHEA IN THE MALE FEMALE

March 1940 -

THERAPY - LOCAL: NONE **ORAL:** SULFATHIAZOLE (Gathrop) Four grams daily for five days

PATIENT LISTING			BACTERIOLOGIC PROGRESS BY WEEKS																FINAL																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																		
AGE	NAME	DATE OF BIRTH	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200	201	202	203	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336	337	338	339	340	341	342	343	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359	360	361	362	363	364	365	366	367	368	369	370	371	372	373	374	375	376	377	378	379	380	381	382	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440	441	442	443	444	445	446	447	448	449	450	451	452	453	454	455	456	457	458	459	460	461	462	463	464	465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515</

† In conversation with the State Board of Health of Missouri.

Fig. 1.—Sample progress chart of 50 cases.

METHOD

The material for a smear is taken from within the urethral canal by means of a platinum loop. A culture is taken from the urethral canal using a sterile cotton applicator. A bivalve speculum without lubrication is used to expose the cervix. A smear and culture are taken as from the urethra. A Gram stain of the smear is made immediately. The culture swabs are immersed in sterile broth until they can be plated on chocolate agar media.

Responsibility for case holding and case finding rests with a medical social worker who has charge of these activities in both male and female gonorrhea clinics. As a result of this joint supervision, a majority of the women under treatment are women named as the source of infection by patients in the associated male clinic.

The new patient is instructed by the physician concerning the nature of her infection, concerning the necessity for treatment, and in the precautions necessary to safeguard others. The patient is encouraged to ask questions about things not clear to her. Logical explanations are given in place of curt "Do's" and "Don't's." We find that time taken to improve education pays in better cooperation.

Each patient is interviewed by the social worker. He makes sure that the patient understands the treatment plan and medical instructions, he studies the social situation and searches for weaknesses that might cause the patient to lapse or interfere with treatment. He assists the patient to adjust herself if she is emotionally disturbed by the diagnosis of gonorrhea, obtains epidemiologic data, and builds up the patient's confidence and good will toward the physician and the clinic. Throughout, emphasis is placed on preventing lapses rather than pursuing the patient after she lapses.

The women in this group are mainly in the second and third decade. The women in our clinic are nearly equally divided between the white and the negro races. A few more are married than single. Eight were known to be pregnant at the time treatment was instituted. None admitted being professional prostitutes. They were all ambulatory patients. Each came for examination, treatment, and returned for observation of her own free will.

We take the usual gynecologic history, make a smear and culture from the urethra and the cervix and a bimanual palpation of the pelvis. The data obtained are recorded on the standard record form of the United States Public Health Service previously mentioned.

Our treatment routine has five divisions: chemotherapy, local therapy, focal therapy, fever therapy, and surgical therapy. Each is used when existing conditions justify such procedure.

Chemotherapy.—After a diagnosis is made, the patient is given sulfathiazole, 1 Gm. four times daily for five successive days. A smear and a culture from the urethra and the cervix have been taken at weekly intervals for three weeks, and at monthly intervals for three months; all six cultures had to be negative before the patient was discharged as cured. Recently the period of observation has been shortened to negative smears and cultures at weekly intervals for six weeks to conform with the recommendations of the Clinical Cooperative Group for Female Gonorrhea adopted at Cleveland in June, 1941. Due allowance is made to avoid examination during menstruation. A single course of the drug given to 110 women gave a cure in 71, a probable cure in 23, failure in 5, and 11 patients never returned. Two could not take the drug as directed because of nausea and vomiting. There were 7 of our patients who had a reappearance of gonococci that we were unable to differentiate, whether they were relapses or reinfections. Each patient was given a second course of sulfathiazole. They remained under observation until our criteria of cure were satisfied. In the group of 23 probable cures, 11 had three negative cultures, 5 had 4 negative cultures, and 7 had 5 negative cultures. If we disregard the probable cures and those that never returned, we have 71 known cures and 5

known failures; this is a cure per cent of 93.4. This result is very gratifying. There is some evidence that inadequate dosage and indiscriminate usage of the sulfonamides may lower the efficiency of sulfathiazole in rendering gonorrhea patients noninfectious.

If a positive culture reappeared before our criteria of cure had been satisfied, the infection was considered a relapse, and hence a drug failure unless there was definite evidence of re-exposure without prophylaxis to a known source of infection.

Local Therapy.—The recourse to local heat, enforced rest, adequate diet, and vaginal irrigations of 0.4 per cent lactic or acetic acid solutions has proved to be of value in acute and subacute infections resistant to chemotherapy. Perhaps the time element alone allowed these women to develop sufficient immunity to destroy their infections. Such a routine was demonstrated as worth while in two of our cases.

Focal Therapy.—Focal therapy is the next logical step in cases of persistent infection after failure of sulfathiazole and conservative local therapy. This includes destruction of the deep glandular tissue of the cervix, Bartholin's and Skene's glands. The popular conization and coagulating technique are effective in sterilizing the types of infection resistant to other forms of treatment. This was necessary in 4 of our cases. We have not yet had to repeat this procedure.

Fever Therapy.—The fourth step in our routine would be controlled sustained fever therapy. As has been previously pointed out by one of us (R. D.), this has been most effective in sterilizing stubborn types of infection resistant to chemotherapy and the accepted local and focal measures. Although it has not been necessary in this series, we suggest prompt utilization of fever therapy without recourse to local or focal therapy if chemotherapy has failed to stop a complicating arthritis or an ocular infection. We do not recommend fever therapy for acute salpingitis or pelvic cellulitis.

Surgical Therapy.—In spite of these improved forms of therapy, women will appear with abscesses of the lower abdomen and pelvis that require surgical drainage. Moreover, the previously outlined therapy will not relieve the semi-invalidism of the individual with a retroverted uterus and prolapsed adnexa bound down by extensive adhesions between the pelvic and abdominal viscera. Radical abdominal surgery is her only hope of relief.

SUMMARY

1. The coordinated effort of a clinician, bacteriologist and medical social worker will improve the management of gonorrhea in women in large clinics.

A joint male and female clinic aids materially in case control.

2. A comprehensive treatment routine is more effective than unplanned haphazard methods.

3. Group recording of results is desirable for statistical evaluation and for comparison of treatment procedures.

4. The use of specialized techniques by qualified personnel is essential to good case holding, case finding, and patient management.

5. Sulfathiazole is a safe and efficient chemical for the treatment of gonorrhea.

A single five-day 20 Gm. course of this drug has given us a cure percentage of 94.9.

Most of the sulfathiazole used in this study was furnished by the Department of Medical Research, Winthrop Chemical Company, New York, N. Y.

4952 MARYLAND AVENUE
607 NORTH GRAND BOULEVARD

DISCUSSION

DR. GRANDISON D. ROYSTON, ST. LOUIS, MO.—I have had the good fortune to observe the work reported by Dr. Smith and to study his careful methods of observation and follow-up work. Dr. Rogers Deakin of the Washington University Department of Urology is doing similar work with gonorrheal infected males, many of whom are consorts of the women treated by Dr. Smith. It is interesting to note that when an infected patient appears in the clinic of one of these men, his or her consort quickly and *voluntarily* appears in the clinic of the other.

Any ambulatory medical treatment for gonorrhea that cures within four to seven days about 94 per cent of those patients treated is a great advance. In cases resisting sulfathiazole, artificial fever therapy (106.6° F. for five hours) should be tried before resorting to any local or surgical procedures, however minor.

It has been found that at a temperature of 105.8° F. (41° C.), 99 per cent of gonococci are destroyed, in an exposure of four to five hours. The remaining 1 per cent of organisms require from eleven to twenty-three hours. This treatment can be exceeded in the human host without injury in the nonpregnant state. The average number of treatments is four, given every fourth day in a hospital with indications and contraindications similar to those for a major surgical procedure.

It must be recognized that tubal infection nearly always means some pelvic peritonitis and often troublesome adhesions. It must also be recognized that an associated cellulitis indicates a mixed infection. Sequelae resulting from these conditions may necessitate surgical intervention even after the eradication of gonorrheal infection.

DR. A. K. PAINE, BOSTON, MASS.—We have been using sulfathiazole at the New England Medical Center for eight months and our experience bears out what Dr. Smith has told us today. The procedure we carry out is that described by Dr. Cooke, namely a total dose of 20 Gm., 3 being given the first day and 2 the succeeding days. We had only two patients with a nausea and vomiting reaction. We made some blood studies and some observations of concentrations of sulfathiazole crystals in the urine but finally discarded both as unnecessary as routine procedures.

Excluding those of the last three months, we have treated 82 patients. Five of these we could not follow leaving 77 cases completely studied. No individuals were treated with sulfathiazole in whom a positive culture was not obtained. These patients have reported for smears and cultures after finishing the sulfathiazole at weekly intervals for one month, and then every two weeks for two months.

Seven of the 77 had positive smears subsequent to the course of treatment. The first one appeared in about two and one-half weeks, the last in three months after treatment. Whether these represent sulfathiazole failures or re-infections is very much a question in my mind. We will always have difficulty, of course, in these cases from the standpoint of reinfection.

DR. WILLARD R. COOKE, GALVESTON, TEXAS.—We have been carrying on a study very similar to this as a part of the work of the committee on gonorrhea in women of the United States Public Health Service. Among the more important things observed was the comparative worthlessness of the smear. Even with our excellent bacteriologic personnel we were unable to get a ratio of better than 1 positive smear to 2.9 positive cultures. We have, however, given up using urethral cultures, because we never got a positive one where there was a negative cervical culture. The best technique of making a culture we found to be the moving of the swab rather vigorously within the cervical canal. We obtained a higher number of positive cultures from direct spreads on the plates without previous broth culture.

As regards the sulfonamides, we had agreed with the committee to use sulfapyridine and are satisfied with it except for the fact that it frequently causes nausea. In such cases we have substituted sulfathiazole, with equally good results. We noted also that it takes longer to obtain a negative culture with sulfathiazole than with sulfapyridine; but there is a much lower incidence of nausea. Another fact about the sulfonamides was that only a small dosage is necessary. Our dosage is 3 Gm. the first day and 2 Gm. a day for nine days thereafter. We made daily cultures and found that with sulfapyridine we got a negative culture on about the third day, and with sulfathiazole on the fourth or fifth day. We have been taught that we should have rather high blood concentrations to obtain effective results, but with the dosage used, checked by a six months' follow-up, we got optimal results with low blood concentrations, frequently under 1 mg. per cent. Therefore, we did not have to subject the patients to potentially dangerous dosages.

We have, however, apparently established the fact of the sulfapyridine-fast organism. Many strains which responded well at first became sulfapyridine-fast subsequently. These cases apparently did not represent the introduction of a new strain of gonococci. We have not satisfied ourselves on the question of reinfection versus relighting of a latent infection. I do not think this can be determined without a study extending over a period of years.

We have now abandoned all local therapy. All of our patients with salpingitis are placed upon chemotherapy, with excellent results in the early cases. On the other hand, we found that the multiple recurrence cases with massive damage to the tube were definitely resistant to chemotherapy. This suggests that we were no longer dealing with a purely gonococcal infection, and that the damage to the tubes was wrought by some sulfonamide-resistant organism.

There has always been an idea that it is difficult to culture the gonococcus. We have not found this to be true. Using a freshly prepared proteose No. 3-hemoglobin-agar, and incubating in a CO₂ atmosphere created by permitting a candle to burn out in a closed can in which the plates were enclosed, we found this procedure very simple. The chief difficulty lies in the rapid deterioration of the culture medium. Mr. Charles E. Lankford, our bacteriologist, has found that by separately tubing the hemoglobin solution and proteose agar in 10 c.c. quantities, a plate may be poured or prepared at one's convenience by melting the agar, mixing the hemoglobin and pouring into sterile plates, thus eliminating this objection, the procedure becoming a very simple one for even the small laboratory.

Another thing we discovered was the relative unreliability of the average laboratory technician's report. We sent positive and negative slides to a number

of laboratories and had them give their technicians a practical examination on these slides. A totally unexpected number of both false negative and false positive reports were returned.

In this study we have cultured every patient going through the gynecologic and obstetric out-clinic. The frequency with which positive cultures are obtained from patients who showed no clinical stigmas of gonorrhea was astounding. In other words, there must be many individuals who are either carriers or have become immune to the gonococcus.

DR. SMITH (closing).—We selected focal therapy in preference to fever therapy in the women with the persistently positive culture from the urethra and the cervix for several reasons. One of these was that in our clinic at the University Dr. Melvin Roblee has been in charge of this work for many years, has used those treatments on well over 1,000 individuals and has not encountered a death. He has had less than 1 per cent morbidity and less than 1 per cent of the patients have had bleeding.

Many of you will agree with Dr. Royston, as I do for some cases, that fever therapy is preferable. For general clinic use, however, I do not believe that we can assist materially with fever therapy the work of the Public Health Service in eradicating infections in those women who would be likely to spread the disease. A very large percentage of those women belong to the lower strata of society that could not afford the treatment and probably would be very hard to manage. If the Public Health Service is correct in estimating some 250,000 new cases each year and if we assume that we are going to have at least a 5 or 6 per cent failure with sulfonamides, we will have some 15,000 individuals who will need further treatment. These would each have to have at least 4 fever treatments, perhaps as many as 6, making a minimum of 60,000 treatments. I do not believe our fever centers could handle them even if they were on the paying basis.

We take a smear as well as a culture at weekly intervals over a seven or eight weeks' observation period. We like to have two negative cultures following menstrual periods. The smear is of value to us, for a diagnosis is thus made immediately, not thirty-six or twenty-four hours later, and the treatment can be instituted at once. I have not used the immediate plating of the swab. Such a practice would possibly answer the problem raised when I have obtained positive smears, and the bacteriologist negative cultures. This combination occurs in only 10 per cent of patients. I believe in general that the continued practice of the clinician examining the smear and the bacteriologist the culture is the best.

AN IMPROVED METHOD OF UTERINE CLOSURE IN HIGH CLASSICAL CESAREAN SECTION*

MILTON G. POTTER, M.D., AND NORMAN W. ELTON, M.D., BUFFALO, N. Y.

(From the Department of Obstetrics of the Millard Fillmore Hospital)

AFTER experience with some 3,500 high classical cesarean sections, we came to believe our prevailing method of suturing could be improved. An exhaustive study of the field impelled us to change our former technique in favor of a simplified method of uterine closure which more happily anticipates and precludes some of the retroactive effects of the prevailing method.

In common with other surgeons of our day, we recognize two methods of cesarean section: the low two-flap, so fashionable today; and the high classical method. This latter has come under considerable question because of the postoperative complications particularly in potentially infected cases and because of the prevalence of rupture. Avoidance of these complications in this operation was our problem.

There were many pitfalls for the surgeon in the latter procedure, wherein he placed three layers of sutures in a terraced manner, one above the other. This method gave the operator a false sense of security; so much so, indeed, that he was likely to ignore the fact that he was strangling tissue between his sutures which might be tied too tightly. If this proved to be the case, there was every chance that infarction of the muscle resulted, and this in turn would allow the lining of the uterus to invaginate into the sloughed-out area, thus weakening the scar.

These complications occurred too frequently to be ignored. It was natural, therefore, in our fortunate position of almost countless opportunities to observe the good and bad features of the, to us, only available method of procedure in cesarean section, for us to give much time and thought to a more effective plan. The result is that we have developed a technical method of closing the uterus which we know after 114 trials constitutes an improvement over the former closure in a high classical cesarean section.

METHOD

Following the incision and the removal of the baby and placenta, the fundus must be held firmly in the left hand of the operator, beneath and behind the incision. Clearly and easily by this means the endometrial border of the incision is exposed and thus the operator with his right hand is enabled to bevel off a portion of the endometrium. Closure of the incision by interrupted silk sutures, is then effected

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

through the outer third of the uterine wall. To facilitate this closure the operator must retain his original grasp of the fundus (in his left hand) while using a long straight, round-pointed needle in his right hand. The sutures, which are spaced about one-fourth of an inch apart, are tied by the assistant, sufficiently tight to hold the parts intact without blanching of tissue. When this is completed, the uterus is dropped back into the lower abdomen. The abdominal cavity is not mopped out, the clots alone are removed, and the intestines, which have been protected by a rubber pad, are not handled. The abdominal incision is then closed in the usual manner with interrupted silk sutures.

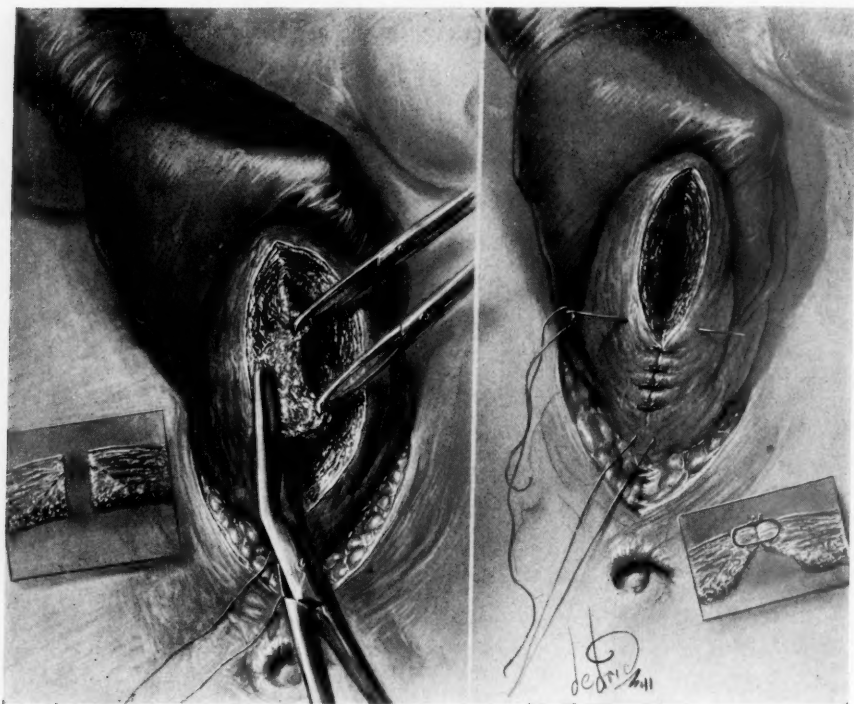


Fig. 1.

DISCUSSION

There have been many favorable factors governing our adoption of this new method. Out of 114 cases, we report 1 death, and in only 3 cases was there a morbidity of 100.4° F. on any two days excluding the first. In absentia are the specters that follow cesarean sections: postoperative nausea, vomiting, and abdominal distention. One of the outstanding clinical facts attending this method, is the marked absence of the usual postoperative bleeding, which was, in the three-layer technique a frequent occurrence. In only one case did we note excessive bleeding, which followed the removal of too much of the endometrial area.

Discussion of this problem reveals that some operators believe this method of closure marks too radical a departure, whereas others main-

tain that the under cutting of the lower border of the incision is unnecessary. The rationale of undercutting or beveling the inner surface of the wound, in addition to simple coaptation by a single row of interrupted sutures not placed deeper than the neutral level, is based upon our conception of defective uterine healing.

We believe that this mechanism of closure involves a play of stresses in the sutured incision above and below a neutral point in the uterine wall. This is characteristic of the mechanics of the shrinkage of a hollow sphere of soft tissue in which the resultant of the forces tends to produce, first, eversion of the wound through retraction of the outer layers, and, second, compression of the inner layers. As this sphere diminishes in size, thickening somewhat during the early phase of the process, the disproportion between the outer and inner layers is markedly accentuated. While the uterus is fully distended at term, there exists little difference between the outer and inner circumference of its mass, but as soon as contraction occurs after delivery, the inner circumference undergoes relatively much greater reduction than does the outer circumference. As a result, although the outer layers can adapt themselves readily to the available space, the inner layers are compressed and crowded into a rapidly diminishing and finally limited space inadequate to their bulk. Under these conditions the forces operating would tend to invert into the wall of the uterus, that portion of the inner layer which might be lying under a weakened part in the wall.

In addition to the stresses active at the site of the uterine incision during contraction after delivery, the damage to the myometrium by strangulating sutures comprises, in our opinion, the principal cause of defective healing following the three-layer technique of suturing. Segments of infarcted muscle may slough for several weeks after the operation, whereas others, remaining in place, undergo hyalinization. Infection, although secondary to tissue change, could occur in any of these wounds. Contamination of the wounds by endometrial implants seems unlikely, since there is small possibility of their survival in necrotic tissue.

The side walls of the wound may roll into the defect or not, depending on when the sloughs fall out. This rolling-in process, provided that sloughed infarcts have dropped out before involution is completed, is most prone to occur during the first days of the puerperium. Whether rolling-in of the endometrium occurs or not, sinus tracts of all shapes and sizes will develop, coming later to be lined by regenerating endometrium. Cross sections of these sinus tracts will appear as islands in prepared sections, but probing of the gross section almost invariably proves that they communicate with the general uterine cavity. Secondary sinus tracts may develop, and should the sinus involve the peritoneum, then the fistula tract, minute or extensive, of the ruptured uterus is created.

We have every reason to believe that our improved method of closure not only corrects the difficulties due to the stresses in the wall of the contracting uterus, but will also prevent strangulation of the muscle. In the presence of infection of any degree, this mode of suture permits free and adequate drainage into the uterine cavity, and it is equally adaptable to potentially septic cases as well as to clean electives. Hemorrhage is prevented by the natural physiologic forces of contraction and involution and should be no more encouraged to occur in the wound than in any other point in the uterus. If the sutures alone were responsible for control of hemorrhage, it is unlikely that the hundreds of venous sinuses exposed by the incision could be shut off effectively by any mode of suture without extreme strangulation of muscle.

This physiologic mode of suture has proved highly adaptable to many situations, including the complete excision of a defective scar in a previous cesarean section. Also, the removal of moderately sized fibroids along the line of the incision is made easy, and the risks of potential sepsis from mismanagement or tardy interference are minimized. Contraction is usually prompt and firm, except in the case when the internal os is obstructed by a segment of membrane; in this case, a clearance of the cervical canal produces the desired effect.

The accuracy in our reasoning regarding tissue healing has been reinforced by numerous observations on healed uterine tissues in other studies. The well-known tendency of the puerperal uterus to turn inside out when incised demonstrates the compressed-spring effect of the inner layers. The difficulty in coaptating the edges of the outer layers after they have been cut longitudinally or after the removal of fibroids provides additional illustration of this eversion tendency.

From our experience we know that suturing only of the outer layer after adequate undercutting of the lower border of the incision, as a part of the operation, must relieve the compression of the inner layers, facilitating contraction, controlling hemorrhage, and reducing the tension on the outer layers, while promoting better coaptation and healing during involution.

Looking down the long and painful road of the cesarean section case, historically speaking, it would seem that our findings in this improved uterine closure exemplify the rule that simple ways and means are best and safest.

DISCUSSION

DR. WILLARD R. COOKE, GALVESTON, TEXAS.—No one can take exception to the fundamental mechanics of this idea. Incision into the active segment of the uterus during cesarean section always leaves the wound lying widely open on account of the greater retraction of the peripheral muscle layers. If the outer layers are brought together the first thing that happens is that the inner surfaces are jammed together, and the other parts of the uterine wall must of necessity lie contiguous to each other.

There are several questions that immediately arise. The first, hemorrhage is apparently of rather rare occurrence. From Dr. Potter's description, that risk is

more than offset by the elimination of the risk of sloughing due to the interruption of circulation. Second, we have an open wound in which there is no mechanical barrier to infection. Yet if infection does invade this open wound, drainage is immediate, and the defense mechanism is better able to take care of the infection than if drainage were interfered with by sutures. The principle is all right but the end results must be determined before the theory can be accepted as definitely proved.

When I read the paper I recalled an observation I once made on some cesarean scars. In two cases of uteri removed by hysterectomy some years after a most meticulous closure by a very expert obstetrician, the scars were terrifying. One exhibited multiple finger-like processes running out into the musculature, while the other was a simple bridge of scar tissue about the thickness of a postal card. Two of the other uteri that came into the laboratory were removed from patients who had been sectioned by a practitioner who never operated when even approximately sober. His method was to put in about three sutures almost anywhere, taking in almost any part of the uterine wall and in these uteri we were unable to find any trace of scar tissue by gross examination.

DR. W. WAYNE BABCOCK, PHILADELPHIA, PA.—The relation of wound reaction and lag in healing to the suture material used has interested me especially during the past ten years. Around catgut used in a wound closure there soon develops an intense polymorphonuclear infiltration within which and close to the catgut is a zone of tissue necrosis. Thus in a wound closed with catgut the early inflammatory and necrotic reaction so delays healing that the union is weakest about the seventh day and there is a tendency to suppuration.

Probably the operator who put only a few sutures in the cesarean wound reduced the reaction and thus had better healing, or perhaps he used silk instead of irritating catgut. In a septic field we have found nothing to equal nonirritating metallic sutures (ends cut very close to the knot) which are not extruded even under suppuration.

It would seem probable that weakness in a uterine wound may depend to a considerable degree on the basis of harmful reactions from the suture material, the reaction being increased by the large number or the large size of the sutures used.

DR. J. W. KENNEDY, PHILADELPHIA, PA.—The late Joseph Price and I have used interrupted through-and-through sutures of silk in the closure of all cesarean sections. There has not been a ruptured uterus following our work, and we have had but one postoperative complication in our experience. This consisted of a small sinus in the lower part of the abdominal incision, through which a few drops of blood would be extruded during each menstrual period.

In my early work I was timid in regard to inserting the suture in the uterine wall and was fearful that it would come in contact with the endometrium, but today our sutures of silk are used as through-and-through interrupted sutures. They are inserted less than 1 cm. apart and a greater amount of uterine structure is included on the peritoneal surface than that of the mucous membrane. This produces a V shape suture in its inclusion of uterine structure, so that there is less inclusion of the uterine wall near the endometrium than on the peritoneal surface. If this plan of suturing is followed, it will avoid the excessive pressure of the internal uterine wall to which Dr. Potter has called our attention.

I know of no location in all surgery where the anatomy of the part is so insulted as that seen in an attempt to divide the uterine wall into muscular and fascial planes, in order that the terrace method of suturing may be applied. It must be remembered that each buried suture is a ligature and has the potential dangers of crushing the tissues and is a foreign body in a dead space undrained.

We use through-and-through sutures of silkworm-gut in all our abdominal work, and there is no record of eventration of the viscera in the history of the institution. Absorbable sutures are never used.

DR. B. Z. CASHMAN, PITTSBURGH, PA.—I would like to ask Dr. Potter whether he has made any study of the scars with this new method of closure?

DR. POTTER (closing).—It was interesting to me in doing these cases and in our former cesarean sections to notice that most of the blood supply of the uterus is found in the outer one-third of the muscle, and it was our attempt in our interrupted sutures to catch those very large sinuses. The control of the hemorrhage which you may have noticed nearer the endometrium is done simply by the coaptation of the wall as the uterus involutes.

We are very pleased with our results with silk. We have been using silk altogether in the past several years, and we feel that it is an ideal drainage suture. We have not been doing this long enough to get specimens of our new scars, only recently I had the opportunity of doing a hysterectomy on a patient on whom I had done a cesarean section with this new method.

GONADOTROPIC HORMONE CONCENTRATION IN EMESIS GRAVIDARUM*

FERDINAND J. SCHOENECK, M.D., SYRACUSE, N. Y.

(*From the Department of Obstetrics, College of Medicine, Syracuse University*)

SEVERAL years ago during the performance of routine diagnostic Friedman tests, it was noted that despite the use of a constant amount of urine, some reactions were much more intense than others. This was interpreted as meaning that some urine specimens contained more gonadotropic hormone than others. On investigation, it was found that most of the intense reactions were obtained with specimens from patients who were nauseated and were vomiting.

These observations suggested a possible connection between the nausea and vomiting of pregnancy and concentration of this hormone. It was decided to make a study along these lines.

A quantitative Friedman test was developed. We determined to find the least possible amounts of urine that would give positive Friedman reactions. It followed naturally that the smaller the amount of urine required to produce a positive reaction, the greater the concentration of hormone. It was felt that such a method might be more satisfactory to our purpose than attempting to isolate and assay the hormone.

Nonpregnant does weighing at least 1,500 Gm. and between sixteen and eighteen weeks of age were used. All animals were of the same or similar breed. Fractional intravenous injections of known pregnancy

*Read at the Fifty-Fourth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 11 to 13, 1941.

Aided by a grant from the Hendricks Research Fund.

urines were made in dilutions of 0.0125 c.c., 0.025 c.c., 0.05 c.c., 0.1 c.c., 0.5 c.c., 1.0 c.c., 3.0 c.c., etc. Two to six rabbits were employed for each test. The animals were laparotomized forty-eight hours after the injections. Corpora hemorrhagica or fresh corpora lutea were the criteria for a positive reaction.

A comparison was made of the minimum amounts of urine necessary to give positive reactions in the various weeks of early pregnancy. Four groups were compared, namely: Group 1, patients absolutely free from nausea or vomiting; Group 2, patients with some nausea and occasional vomiting, the so-called "physiologic vomiting of pregnancy"; Group 3, patients with excessive nausea and vomiting; and Group 4, definite pernicious vomiting of pregnancy. All the patients were observed personally and classified according to the above groups.

TABLE I

WEEKS	URINE (C.C.)			
	NO NAUSEA OR VOMITING	PHYSIOLOGIC NAUSEA AND VOMITING	EXCESSIVE NAUSEA AND VOMITING	PERNICIOUS VOMITING
5	1.8 (7)	0.5 (1)	0.5 (1)	
6	1.2 (8)	0.66 (3)	0.037 (2)	0.025 (1)
7	0.49 (11)	0.085 (7)	0.05 (1)	0.025 (3)
8	0.41 (5)	0.24 (8)	0.047 (3)	
9	0.50 (8)	0.16 (11)	0.121 (7)	0.018 (4)
10	0.35 (8)	0.23 (9)	0.047 (5)	0.019 (3)
11	0.5 (4)	0.45 (13)	0.04 (5)	0.027 (2)
12	0.45 (7)	0.39 (4)	0.05 (1)	0.025 (1)
13	0.83 (3)	0.5 (2)		
14	1.08 (6)	0.5 (2)		0.05 (1)
15	1.1 (5)	0.3 (2)		

The results of 173 quantitative urine tests are charted in Table I. Of these, 72 specimens were from patients with no nausea or vomiting; 62 in the group of physiologic vomiting; 24 excessive nausea and vomiting; and 15 pernicious vomiting. The number of tests for the various weeks of pregnancy is shown in the upper right hand corner of each box.

TABLE II

WEEKS	BLOOD SERUM (C.C.)			
	NO NAUSEA OR VOMITING	PHYSIOLOGIC NAUSEA AND VOMITING	EXCESSIVE NAUSEA AND VOMITING	PERNICIOUS VOMITING
5	0.5 (3)			
6	0.6 (5)	0.05 (1)	0.025 (1)	
7	0.27 (6)	0.045 (5)		0.025 (1)
8	0.10 (2)	0.062 (6)	0.05 (1)	
9	0.09 (5)	0.05 (7)	0.04 (5)	0.020 (3)
10	0.083 (9)	0.035 (5)	0.035 (5)	
11	0.075 (2)	0.122 (8)	0.037 (2)	0.05 (1)
12	0.1 (2)	0.05 (1)		
13	0.1 (2)	0.05 (1)		
14	0.42 (5)	0.5 (1)		
15	0.1 (2)	0.05 (1)		

The figures show the average amount of urine required to give positive reactions in cubic centimeters. A study of this chart shows that the greater the degree of nausea and vomiting, the smaller is the amount of urine required to produce positive reactions. Hence, it can be concluded that there is an increased concentration of gonadotropic hormone in the urine of patients with nausea and vomiting.

We have carried out a similar set of quantitative experiments on blood serum. Table II shows the results of 101 quantitative serum tests. The results are practically the same as with the urine determinations. There are a few exceptions, namely, in the ten-week group the average amounts

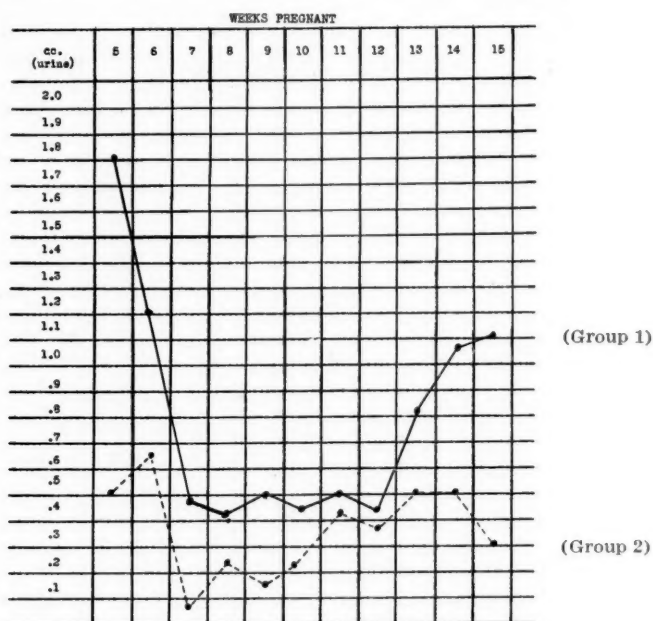


Fig. 1.—Chart showing fractional Friedman tests.

in Groups 2 and 3 are the same; in the eleven-week group, there is an average discrepancy between Groups 1 and 2; also in the fourteen-week group the average amounts in Groups 1 and 2 are approximately the same. However, in general it would seem fair to say that the serum studies confirm the findings of the studies on the urine specimens.

There is naturally one essential question that arises in this study. Is the increased concentration of gonadotropic hormone in the vomiting cases a true one, or is it simply the result of concentration due to dehydration resulting from the loss of fluids associated with the vomiting.

We are convinced from previous studies that simple concentration can be ruled out from the viewpoint of specific gravity determinations.

In order to further elucidate this particular phase, we have, in recent months, concentrated our studies on a comparison between Group 1, i.e.,

patients with no nausea or vomiting, and Group 2, i.e., physiologic nausea and vomiting. We feel quite certain from clinical observation of the latter group that there was not sufficient nausea and vomiting to upset the water balance. We believe, therefore, that the question of dehydration can be eliminated in a comparison of these two groups.

The findings of the urine studies (Fig. 1) demonstrate that less urine is required to produce positive reactions with the group of physiologic nausea and vomiting than is necessary in the group without these symptoms. This seems to justify the contention that simple concentration due to dehydration does not account for the findings.

DISCUSSION

We have presented evidence to show that there is an increased concentration of gonadotropic hormone in the urine of pregnant patients who present the symptoms of nausea and vomiting as compared to pregnant patients who are free from these symptoms. Similar evidence from studies with blood serum, in general, corroborates the urine studies.

One other observation seems pertinent. It is generally conceded that the greatest concentration of gonadotropic hormone is present from the sixth to the twelfth or thirteenth week of pregnancy. This is the same period of pregnancy during which clinical observation shows nausea and vomiting to be most commonly encountered. This relationship is probably significant.

The evidence presented is not necessarily conclusive that there is an etiologic relationship between increased gonadotropic hormone production and the nausea and vomiting of pregnancy. However, it is felt that sufficient data have been offered to allow speculation that there may be some relationship between a hormone disbalance and these commonly encountered symptoms. Certainly no satisfactory explanation has yet been presented to account for the early toxemias of pregnancy. We suggest, therefore, that the evidence presented may offer a possible explanation which future observations will prove or disprove.

REFERENCES

- Friedman, M. H., and Lapham, M. E.: *AM. J. OBST. & GYNEC.* 21: 405, 1931.
 Schoeneck, F. J.: *Proc. Soc. Exper. Biol. & Med.* 32: 357, 1934.
 Schoeneck, F. J.: *AM. J. OBST. & GYNEC.* 32: 104, 1936.

103 MEDICAL ARTS BUILDING

DISCUSSION

DR. EMIL NOVAK, BALTIMORE, MD.—Dr. Schoeneck's work is of interest in its relation to the original investigations of Smith and Smith, which indicated a relative excess of chorionic hormone and a deficiency of estrogen in pregnancy toxemias. It appears, too, to indicate the role of the trophoblast in the production of gonadotropic principles, and might suggest the possible role of trophoblastic dysfunction, in the production of certain toxemias of pregnancy. Our knowledge is still too meager to draw any definite conclusions, and such efforts as have been made to apply these investigations therapeutically have thus far yielded rather disappointing results.

DR. ALBERT W. HOLMAN, PORTLAND, ORE.—I would like to suggest that in future work along this line the spinal fluid content be examined. In the reference to pernicious vomiting I believe the dilution was to 0.025 c.c. With hydatid mole the concentration of hormone is much higher and quantitative tests are positive in even lower dilutions. We know that in hydatid mole the spinal fluid content is positive, and I am wondering if in the serious cases of pernicious vomiting the spinal fluid estimation would be positive.

DR. SCHOENECK (closing).—Dr. Novak's remarks, of course, as to the practical application of these findings are very true. If our experiments are confirmed, however, it would seem that clinically we should administer large amounts of follicular hormone. This, of course, might be dangerous.

In reply to the remarks about the spinal fluid estimations, I suppose that can be done but I think it would be impractical with the method that we have evolved. I believe we could not get sufficient spinal fluid from the individual patient to make a practical test.

BLOOD TRANSFUSIONS IN PREGNANCY

A REVIEW OF 3,000 CASES

E. G. HAMILTON, M.D., AND A. P. MARTINI, M.D., ST. LOUIS, MO.

(From St. Mary's Group Hospitals and the Department of Obstetrics & Gynecology,
St. Louis University School of Medicine)

UNTIL recently the dangers inherent in blood transfusions have not been emphasized. The early literature contains reports of a large number of reactions due to gross errors in typing, to failure to cross match, and to generally poor technique. As methods improved and the number of reactions decreased, more and more transfusions were given. The element of danger came to be disregarded. Recently, however, reports have appeared to suggest that severe reactions do occur even with improved technique.^{16, 27}

Within the last two years the dangers associated with transfusions have been brought to our personal attention by a number of incidents. Since all the severe reactions occurred in association with pregnancy, we suspected that it in some way predisposed to incompatibilities.

Even an incomplete review of the literature reveals a number of transfusion reactions in pregnancy in which no incompatibility was demonstrated by the routine methods.

Culbertson and Ratcliffe⁶ found two Group O patients with atypical agglutinins, both of which were in the puerperium. The authors call attention to the fact but attach no significance to it. Later, Levine and Stetson reported a case of intragroup agglutination and were the first to suggest that a mother could be immunized by a fetus carrying antigens inherited from the father.¹⁷ Jonsson¹³ found the average titer of Isohemolysins a and b to be higher than normal in women who had recently given birth. He attributes this finding to specific stimulation provided in cases of heterospecific pregnancy. For example, the presence of a Group A or B fetus in a Group O mother can produce a rise in the titer of Isoantibodies a and b, respectively.

Subgroups A₁ and A₂ and also A₁B and A₂B have been described and are known to cause mistakes leading to reactions⁸ but no fatalities have been attributed to these subgroups. And there are also other antigenic factors in the human blood which may cause reactions or the production of antibodies.

Of particular interest are the recent publications of Levine¹⁸ and Burnham⁵ in which the etiology of erythroblastosis fetalis has been established. They have called attention to the high incidence of severe transfusion accidents in mothers of erythroblastic babies. The Rh factor, present in the blood of the *Macacus rhesus* monkey and in 86 per cent of all human bloods of the white race, is inherited as a dominant property similar to the A and B factors of the four blood groups.

They have shown that an Rh negative woman carrying an Rh positive baby may, in certain cases, form anti-Rh agglutinins which pass

TABLE I

AUTHOR	AGE	CONDITION	BLOOD TYPES		PRELIM. CROSS-MATCHING	CHECK	AMT. GIVEN	TYPE OF REACTION	CONFIRMED AT AUTOPSY
			RECIP.	DONOR					
Culbertson and Ratcliffe ⁶	?	Dystocia, cesarean section	0	0	Compatible	Atypical agglutinins	?	Chill, temp. rise to 105° F. Anuria, N.P.N. up to 235 Mg. %. Recovered. Husband was the donor	
Daniels, Leonard, and Holtzman ⁷	28	Terminated abortion became incomplete	0	0	Compatible	Compatible	250 c.c.	Chill, moderate temperature rise. Uremia, died 8 da. after transfusion	Typical findings in the kidney
DeGowin ⁹ Case 8	25	Post-partum sepsis	AB	0	Donor's serum agglutinated patient's cells	Same	125 c.c.	Hemolytic react. without renal insufficiency. Feeling of constriction in chest. Patient lived	
DeGowin Case 10	26	Pyelitis of pregnancy	B	B	Compatible	Compatible	500 c.c. 500 c.c.	Second transfusion 19 days after first. Next day patient jaundiced. Second day delivered premature infant. Patient recovered	
Johnson and Conway ¹² Case 3	22	3 month pregnancy. Bleeding	?	?	Compatible	Compatible	500 c.c.	Hemolytic reaction. Died in uremia 18 days after transfusion	Focal areas of hemorrhage and necrosis in the liver. Typical kidney changes
Bordley ³ Case 7	36	Ruptured ectopic	0	0	?	?	?	Died in uremia on ninth day after transfusion	Liver: numerous areas of hemorrhage and necrosis mostly about the center of the lobe. Kidney: typical changes

Bordley ³ Case 8	32	Ruptured ectopic	A	A	Compatible	Compatible	?	No immediate reaction. Died in uremia on sixth day after trans- fusion	Liver: central necrosis. Kidneys: hematin in tubules
Bordley ³ Case 9	30	Ruptured ectopic	?	?	?	?	?	Died in uremia on eighth day after trans- fusion	
Bordley ³ Case 15	29	Anemia follow- ing pregnancy	A	A	Compatible	?	?	Blood urea to 354 Mg. %. Died in uremia on eleventh day after transfusion	Typical kidney change
Brines ⁴ Case 2	20	3 month preg- nancy. Vomit- ing. Thera- peutic abor- tion	0	0	Compatible	Compatible	500 c.c.	Gasped, became cya- notic and died 2 min- utes after transfu- sion. Husband was the donor	No explanation for the sudden death. Acute syphilitic myocarditis with coronary arteri- tis
Bancroft ¹	49	Incomplete abortion	Not given	Not given	Compatible	Compatible	400 c.c.	Chill lasting 20 min., temp. 103.4° F. Anu- ria for 9 days. Re- covered following de- capsulation of the kidneys	
Levine, Katzin, and Burn- ham ¹⁶ Pt. R. C.	32	Pregnant	0	0	Compatible	Atyp. agglu- tinins few days later	?	Patient went into uremia but recovered. Husband was the donor	
Pt. E. F. W.	38	Preeclampsia	0	0	Compatible	Same as above found on sixth day	?	Icterus, oliguria and Nitrogen retention— Recovered. Fetus had erythroblastosis fetalis. Husband was the donor	

TABLE I—CONT'D

AUTHOR	AGE	CONDITION	BLOOD TYPES		PRELIM. CROSS-MATCHING	CHECK	AMT. GIVEN	TYPE OF REACTION	CONFIRMED AT AUTOPSY
			RECIP.	DONOR					
Levine, Katzen and Burnham Pt. F. Z.	?	Placenta previa, cesarean, mac- erated fetus	?	?	Compatible	Type of agglu- tinins found just before death	?	Chill, fever, anuria, died in uremia 12 days after transfusion	
Pt. G. B.	32	Cesarean, fetal hydrops	A	A	Compatible	As above found on fourth day	?	Same as above, died on ninth posttransfusion day in uremia. Hus- band was the donor	
Pt. J. B.	30	Pregnant	?	?	Compatible	Compatible	?	Same as above, died on ninth day after trans- fusion in uremia	
Mandelbaum ²⁰	38	Pregnant B. P. 276/160	A	A	Compatible	Donor-A ₁ , Pt.-A ₂	500 c.c.	No chill or fever. Anu- ria, icterus, petechiae, and pruritus. N.P.N. went to 262 Mg. %. Patient recovered. Husband was the donor	
Bordley ³ Case 18	?	Ruptured ectopic	Given an auto transfusion				500 c.c.	Died in uremia 6 days after transfusion	
Parr and Kirch- ner ²¹	27	Menorrhagia, 6 wk. post-abor- tal	0	0	Compatible	Slow hemolysis of donor's cells in recipi- ent's serum	400 c.c.	Vomited blood, hemat- uria, bled from nec- dle wounds. Died four hours after transfu- sion. Husband was the donor	None reported

Goldring and Graefn Case 2	25	Abortion	0	0	?	Compatible Compatible Compatible	500 c.c. 360 c.c. 500 c.c.	7-9-32 7-10-32 8-6-32 (Husband) Following blood from husband, 4-plus albumin, hematuria, N.P.N. to 180. Recovered	
	24	Possible abortion	0	0	Compatible	Not done	400 c.c.	Died in uremia 14 days after transfusion	No autopsy
	24	Possible ectopic	0	0	Compatible	Compatible	500 c.c.	Chill, pain in back, anuria, and jaundice. Recovered	
Daniels, Leonard, and Holtzman?	28	Long labor, high forceps retained placenta	0	0	Compatible	Not done	500 c.c.	No immediate one mentioned. Hematuria, uremia, died 4 days after transfusion	Typical kidney changes, only congestion in the liver
Idem	43	Spontaneous abortion	B	B	Compatible	Right type after 20 min., Hemol. of donor's cells by patient's serum	500 c.c.	Palpitation, flushing, nausea, vomiting, chilliness and mild temperature rise. Oliguria for 4 days N.P.N. up to 117 Mg. %. Patient recovered	
Idem	25	Incomplete abortion	?	?	Compatible Compatible	Not done Not done	500 c.c. 500 c.c.	Temperature rise. Severe chill, temperature to 105.6° F. Jaundice. Died in uremia on ninth day after second transfusion	No autopsy reported—second transfusion given 9 days after first. Time for antibodies to have developed from the first transfusion
Idem	32	Abortion	A	0	Compatible	Not done	500 c.c.	As second above. Died 6 days after transfusion	None reported

back through the placenta to destroy the baby's blood. This Rh factor is thought to be responsible for about 90 per cent of all intragroup transfusion accidents after repeated transfusions or in pregnancy at the first transfusion.

It is also probable that the Rh factor causes many of the reactions between different groups that seem compatible by the Landsteiner method of cross-matching.

Furthermore, the pregnant woman and especially the toxemic one with her fatty liver, has poor protection against transfusion incompatibilities. In the case of hemolytic reactions the kidney of the pregnant woman, and especially of the toxemic one, is particularly vulnerable. The precipitation of hematin in already swollen tubules could quite possibly result in a fatal anuria, whereas an equal amount precipitated in a previously normal kidney might not be fatal.

A number of severe transfusion reactions have been collected from the literature. It is our opinion that scores of similar reactions have occurred unrecognized. Our own fatal cases were not recognized as such during life. The thought that others have had similar experiences is given credence by the report of a case at the Massachusetts General Hospital by Mallory.¹⁹ The patient (not pregnant) presented a picture which in retrospect was typical of a fatal blood transfusion reaction. Yet the pathologist's report of a blood transfusion death came as a complete surprise.

In Table I are collected 26 severe transfusion reactions occurring in pregnancy or the puerperium. Of this number, 16 died and 6 showed typical kidney changes. It will be seen that in 7 of the cases the reaction was caused by the husband's blood, even though in every case both parents belonged to the same blood group. Of special interest is the case of ruptured ectopic pregnancy reported by Bordley. This patient was given 500 c.c. of blood from her own abdominal cavity, and died in uremia six days later. In this instance one must consider the possibility that the patient had become sensitized to the fetus. This might occur in two ways. First, antigens in the fetal blood reaching the maternal circulation through a destroyed placental barrier could stimulate antibody formation in the mother. And second, absorption of antigens by the peritoneum could produce a similar result. It is doubtful if hemolyzed blood, otherwise compatible, would produce such a severe reaction. Tiber²⁴ mentions a similar instance. In 123 cases of autohemotransfusion there was 1 transfusion death. In 66 cases of ectopic pregnancy given both direct and autohemotransfusions, there were two transfusion deaths. In all instances rupture occurred more than seventy-two hours prior to transfusion. This incidence of transfusion deaths is extremely high.

The fact that re-cross-matching was not done in nine of the cases is an indication that a transfusion reaction was not thought of at the time.

On our obstetric and gynecologic services both minor and severe reactions came in such rapid succession that we became loath to order a

transfusion even when strongly indicated. In other departments, transfusions were given with relative impunity. A survey was consequently made of 3,000 transfusions given in the last three and one-half years in the St. Mary's Group Hospitals of St. Louis. Our findings are given in Tables II to IV.

TABLE II. SHOWING GREATLY INCREASED INCIDENCE OF TRANSFUSION REACTIONS AMONG THOSE GIVEN TO PREGNANT PATIENTS OVER THOSE GIVEN TO NONPREGNANT ONES

	NUMBER OF TRANSFUSIONS	NUMBER OF REACTIONS	PER CENT OF REACTIONS
To nonobstetric cases	2,604	299	11.4
To obstetric cases	396	82	20.9
To all cases	3,000	381	12.7

TABLE III. INDICATING INCREASED INCIDENCE OF TRANSFUSION REACTIONS AMONG PREGNANT PATIENTS

	NUMBER OF PATIENTS	NUMBER REACTED	PER CENT REACTED
Nonobstetric cases	1,108	215	19.4
Obstetric cases	151	61	40.6
All cases	1,259	276	22.0

TABLE IV. SHOWING INCIDENCE OF TRANSFUSION REACTIONS WHEN THE HUSBAND WAS THE DONOR AS COMPARED TO OTHER DONORS. IN OUR SERIES THERE IS NO SIGNIFICANT DIFFERENCE

	NUMBER OF TIMES	NUMBER OF REACTIONS	PER CENT OF REACTIONS
Husband donor	40	9	22.5
Other donors	356	73	20.5

In the entire series 313 bank blood transfusions were given with 57 (18.2 per cent) reactions. The balance was citrate transfusions with 324 (12.7 per cent) reactions. As here enumerated, reactions consist of urticaria, or a chill and at least a 1° (F.) rise in temperature. Urticarial reactions alone were evident in 50 out of 381 reactions.

CASE HISTORIES

CASE 1.—Patient, D. K. (No. 40-1257), aged 24, para i, gravida ii, entered the hospital in labor with a blood pressure of 145/102 mm. Hg; she delivered a one-month, premature living baby after a twelve-hour labor. There was minimal blood loss but patient went into shock. The patient, Type A, was given 1,000 c.c.* of bank blood from an O donor. An hour after the transfusion started the patient had a chilly sensation and nausea, with temperature rise to 102.8° F. axillary two hours after the transfusion. The patient failed to respond and another transfusion (donor Type A) was given with no reaction. During the next forty-eight hours, the blood pressure remained between 66/32 and 94/70. There followed decreased urinary output during the next six days, the nonprotein nitrogen rising to 83 mg. per cent on the fourth day. On the second day icterus index was 26. The red blood count dropped from 3,930,000 immediately after the second transfusion, to

*One thousand cubic centimeters of bank blood contains 400 c.c. of blood and 600 c.c. of dextrose citrate solution.

2,730,000 four days later. The urine contained 1- to 3-plus albumin and microscopic blood up to the fifth post-partum day. Patient recovered and returned home on the twenty-sixth post-partum day. Cross-matching was not repeated.

CASE 2.—Patient N. V. (No. 39-18029), aged 29 years, para i, gravida ii, entered the hospital two weeks before term with vaginal bleeding that was found to be due to partial placental separation. Patient, Type B, was given 400 c.c. of citrated blood from a B donor. Ten days later 1,000 c.c. of bank blood were given from a B donor, followed by a chill, temperature rise from normal to 103° F., drop in blood pressure from 90/60 to 60/40, emesis of bright red blood, and fetal heart tones, which had been present before the transfusion, could no longer be heard. A diagnosis of premature separation of the placenta was made and confirmed at a cesarean section done under local anesthesia. A dead child was delivered. The mother died on the eighth postoperative day of a *B. welchii* bacteriemia. But the nonprotein nitrogen steadily rose to 120 mg. per cent two days before death, the urine contained occult blood and two-plus albumin and with decreased urinary output. In addition to her infection this patient undoubtedly had a severe transfusion reaction which, of itself, may or may not have otherwise caused death. There was no autopsy, and no re-cross-matching.

CASE 3.—Patient C. D. (No. 40-468), aged 26 years, entered the hospital two weeks past term. The patient, Type AB, after a thirty-six-hour labor was delivered of a 9½ pound living baby by cesarean section. Before the patient roused from the operation she was given 1,000 c.c. of bank blood, Type O, and no immediate reaction was noted. Four hours later the temperature was 103° F. The urinary output was diminished and the nonprotein nitrogen rose to 150 mg. per cent the day before death, which came on the eighth postoperative day. The urine contained two plus albumin, 15 to 20 red blood cells per high power field and granular casts.

Essential Pathologic Findings.—*Gross:* Liver: Weight 1,750 Gm. Liver showed on cut section focal areas of hemorrhage and congestion in the area of the central vein. Kidneys: Each weighed 200 Gm. There was evidence of swelling, no evidence of infarction; cortex, calices and pyramids showed no abnormalities. *Microscopic:* Liver: Focal areas of congestion, degeneration, atrophy and necrosis of the liver cell cords that appeared quite constantly about the central vein (see Fig. 1). Kidney: Most of the glomeruli showed little morphologic change, though the tuft was frequently shrunken, and Bowman's spaces contained amorphous material in round pale bodies suggestive of hemolyzed red blood cells. The epithelium of the convoluted tubules showed a mild degenerative (nephrotic) change. In the medulla, the collecting tubules were almost all filled by amorphous, granular or hyaline material. In some, red blood cells were present (Fig. 2).

CASE 4.—Patient M. S. (No. 40-4559), Type O, aged 35 years, para i, gravida ii, entered the hospital about the thirtieth week for a cesarean section because of a blood pressure of 180/105 mm. Hg and an extensive retinal hemorrhage. The first pregnancy had been complicated by hypertension of 180/100, two-plus urinary albumin and a section for primary uterine inertia. Immediately after the second cesarean section she was given 500 c.c. of citrated Type O blood which was

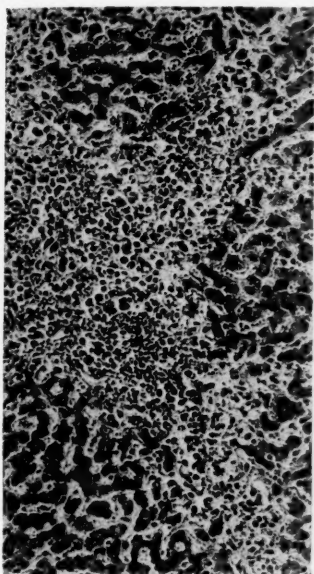


Fig. 1.



Fig. 2.



Fig. 3.

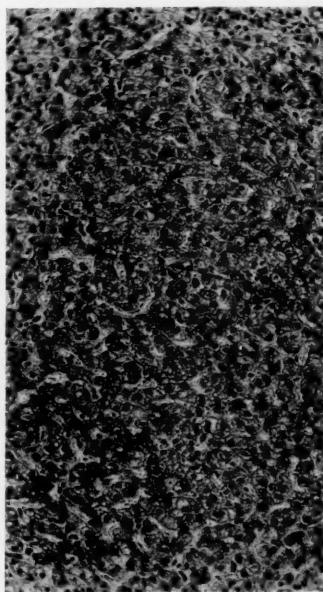


Fig. 4.

- Fig. 1.—Case 3. Liver, showing focal areas of congestion, degeneration, atrophy and necrosis about the central vein. ($\times 140$.)
 Fig. 2.—Case 3. Kidney, hemolyzed red blood cells in the convoluted tubules. ($\times 140$.)
 Fig. 3.—Case 4. Kidney, hemoglobin casts in the kidney tubules. ($\times 140$.)
 Fig. 4.—Case 4. Liver. Thickening and swelling of liver cord cells, no areas of necrosis. ($\times 140$.)

followed by a chill and a temperature of 101.6° F. On the following day the patient was given 500 c.c. of citrated blood from a Type O donor with no reaction. Because the patient failed to get the usual benefit from the preceding transfusion, another 500 c.c. of citrated, Type O, blood were given five days later, and were followed by a chill and a rise in temperature up to 101.2° (rectal) from normal. Three days later 250 c.c. of citrated Type O blood were given and repeated the following day, both without reaction. The patient gradually became jaundiced, the red blood count and hemoglobin fell in spite of the transfusions, and the nonprotein nitrogen rose to 200 mg. per cent when the patient died on the eleventh postoperative day. Urine showed albumin 2- to 3-plus, red blood cells, and hyaline and granular casts. There was the usual depression of fluid output which was returning just before death.

Pathologic Report.—*Gross:* Liver: Normal size, firm in consistency, smooth, and on cut section showed a yellow homogenous appearance. Kidneys: Approximately two times normal size. Weight of both 500 Gm. Capsule stripped easily and displayed smooth surface, mottled in appearance. On cut section these mottled areas could be seen in the cortex. *Microscopic:* Kidney: H and E stains showed marked tubular degeneration. There was marked granularity and swelling of the cells of the proximal convoluted tubules, with hemoglobin casts found in both in the convoluted tubules and tubules elsewhere (Fig. 3). Liver: There were no well-defined areas of engorgement or thrombosis of the sinusoids, and there were no definite areas of liver cell necrosis (see Fig. 4).

DISCUSSION

It has been our experience that transfusion reactions are common in pregnancy and the puerperium. A number of cases from the literature are presented which are similar to ours. It is our opinion that a careful study of all transfusions in pregnancy will reveal a great number of reactions hitherto attributed to some other cause.

In none of our fatal cases was a transfusion reaction recognized before death. This is unfortunate because valuable determinations remained undone. One of our fatal cases (C. D.) was transfused before she had been roused from the operation and no chill was observed. In two of the others, the immediate reaction was not more severe than any number of ordinary transfusion reactions without serious sequelae. This fact often is responsible for failure of physicians to recognize that the patient has received incompatible blood.

In our series of 3,000 transfusions, the percentage of reactions, both mild and severe, was higher in the pregnant patients. Since all these transfusions were administered under similar conditions, it would appear that pregnancy presents certain phenomena which make it more difficult to transfuse safely. Among these phenomena, the following should be considered:

1. Anemias of pregnancy or those resulting from abortions may lead to errors of grouping through "pseudo-agglutination."²² The strain on an anemic myocardium due to a severe rigor superimposed upon an increased blood volume may result in a fatality.

2. Infections, as seen in puerperal sepsis, have long been known to carry a high percentage of reactions.

3. Patients with kidney damage, both glomerular and tubular, also have a high percentage of reactions. This applies to the toxemias of pregnancy.

4. Atypical agglutinins have recently been shown to cause severe or even fatal reactions. It has also been shown that in pregnancy the proportion of patients with these agglutinins is unusually high.

One or more of these factors may be present in a given case. Only by early recognition of the reaction can the cause of the incompatibility be determined. An investigation in a suspected case of incompatibility should include the following tests:

1. Re-cross-matching of the original blood samples, using the method of Levine.¹⁸

2. Re-cross-matching following the reaction. If no incompatibility is found, it may be that the agglutinin is absorbed by the donor's blood. Or an agglutininogen may be absorbed by the recipient's blood. A re-check in four days or more will reveal the error.

3. Determine if the Rh factor or subgroups of A or AB are responsible, if this is possible.

4. Careful check of apparatus, methods of collecting and administration, and titers of test sera.

5. Daily examination of the urine for microscopic and occult blood. Icterus index, serum bilirubin and Hb determinations, accurate fluid summary, and frequent temperature and blood pressure readings.

Certain implications are apparent from the foregoing. The indiscriminate giving of blood in pregnancy is deprecated. We hasten to add that we do not condemn the use of transfusions in pregnancy. We recognize it as one of our most valuable therapeutic weapons. Occasions arise where the urgency for blood is so great that atypical reactions cannot be considered. But oftentimes in cases of mild shock with moderate blood loss, in the toxemias of pregnancy, and postoperatively, intravenous glucose or plasma may serve the same purpose with less danger. In any case where time permits, every precaution should be taken to detect incompatibilities. The usual cross-matching should be replaced by the centrifuge method of Levine,¹⁸ in which the patient's serum and donor's cell suspension are incubated for thirty minutes at 37° C. and then centrifuged at low speed (500 r.p.m.) for one minute and read as in the usual Landsteiner method. The laboratory should be notified that the patient is a "pregnancy case" and should take special care in the selection of donors. The alkalization of the urine to prevent the precipitation of acid hematin in the kidney tubules has been found helpful and should be used. In the toxemias, potassium bicarbonate is suggested.

The phenomenon of sensitization of the mother to the fetus brings out some interesting speculations that may be of greatest importance and which require further investigation.

In his book on *Abortion*, Taussig²³ states that a tendency to abortions has been observed where there was a difference in the blood groups of

husband and wife. Levine, Katzin, and Burnham¹⁶ in their discussion on the possible bearing of iso-immunization on the etiology of erythroblastosis fetalis, mention habitual abortions and premature death of the fetus in several instances.

As long ago as 1905, Dienst¹⁰ touched on this phenomenon as a possible cause of eclampsia. It is known that a woman, carrying a fetus which has inherited certain antigens from the father which are absent in herself, may become sensitized to her child. Chorionic villi with patent capillaries have been found in the maternal circulation. It is therefore not difficult to conceive of a series of blood transfusions in miniature in which small amounts of fetal blood enter the maternal circulation. Levine and his associates indicate that antigens and antibodies may pass through the intact placenta. As the titer of antibodies in the mother rises, the reaction to fetal blood or fetal antigen increases. The similarity of the liver and kidney pathology in eclampsia and in transfusion deaths is striking. The former may be considered a chronic condition, the latter an acute episode. Further investigation will determine whether repeated small transfusions of incompatible blood will cause thickening of the glomerular basement membrane, which is the one distinguishing renal lesion in eclampsia.²

CONCLUSIONS

1. The pregnant or puerperal woman is more susceptible to all types of transfusion reactions.
2. In a series of 3,000 transfusions there were 12.7 per cent reactions. In 396 transfusions given to obstetric patients, there were 20.9 per cent reactions, whereas there were reactions in only 11.4 per cent of the non-pregnant cases. Of all the obstetric patients transfused, 40.6 per cent had reactions, while only 19.4 per cent of the nonpregnant patients reacted.
3. From the material found in the literature, we feel that it is probably safer not to use the husband as a donor without special compatibility tests. However, in our series the increased incidence of reactions was not significant.
4. Four severe transfusion reactions are reported. All occurred in association with pregnancy, and there were two deaths with autopsy.
5. Except in emergencies, the selection of donors should be made with special care and the patient prepared for transfusion by alkalization.
6. A procedure is suggested for investigating suspected cases of transfusion reaction.
7. The phenomena underlying the increased incidence of transfusion reactions in pregnancy have been shown to cause erythroblastosis fetalis and may produce certain toxemias of pregnancy.

We wish to thank Dr. William C. Stude for the use of one of these cases and Dr. Grey Jones for the use of a case and for his helpful suggestions. We also wish to thank the Department of Pathology for their cooperation in this work.

REFERENCES

1. Baneroff, F. W.: *Ann. Surg.* **81**: 733, 1935.
2. Bell, E. T.: *Am. J. Path.* **8**: 1, 1932.
3. Bordley, James, III: *Arch. Int. Med.* **47**: 288, 1931.
4. Brines, C. A.: *J. A. M. A.* **94**: 1114, 1930.
5. Burnham, L.: *AM. J. OBST. & GYNEC.* **42**: 389, 1941.
6. Culbertson, C. G., and Ratcliffe, A. W.: *Am. J. M. Sc.* **192**: 471, 1936.
7. Daniels, W. B., Leonard, B. W., and Holtzman, S.: *J. A. M. A.* **116**: 1208, 1941.
8. Davidson, I.: *J. A. M. A.* **112**: 713, 1939.
9. DeGowin, E. L.: *Ann. Int. Med.* **11**: 1777, 1938.
10. Dienst, A.: *Zentralbl. f. Gynäk.* **29**: 353, 1905.
11. Goldring, W., and Graef, I.: *Arch. Int. Med.* **58**: 825, 1936.
12. Johnson, R. A., and Conway, J. F.: *AM. J. OBST. & GYNEC.* **26**: 255, 1933.
13. Jonsson, B.: *Acta Path. et Microbiol. Scandinav.* **13**: 424, 1936.
14. Landsteiner, K., and Wiener, A. S.: *Proc. Soc. Exper. Biol. & Med.* **43**: 223, 1940.
15. Levine, P., and Katzin, E. M.: *Proc. Soc. Exper. Biol. & Med.* **45**: 343, 1940.
16. Levine, P., Katzin, E. M., and Burnham, L.: *J. A. M. A.* **116**: 825, 1941.
17. Levine, P., and Stetson, R. E.: *J. A. M. A.* **113**: 126, 1939.
18. Levine, P.: *AM. J. OBST. & GYNEC.* **42**: 165, 1941.
19. Mallory, T. B.: *New England J. Med.* **220**: 928, 1939.
20. Mandelbaum, H.: *Ann. Int. Med.* **12**: 1699, 1939.
21. Parr, L. W., and Kirchner, H.: *J. A. M. A.* **98**: 47, 1932.
22. Polayes, S. H., and Lederer, M.: *J. Lab. & Clin. Med.* **17**: 1029, 1932.
23. Taussig, F. J.: *Abortion, Spontaneous and Induced*, St. Louis, 1936, The C. V. Mosby Co., p. 100.
24. Tiber, L. J.: *California & West. Med.* **41**: 16, 1934.
25. Todd and Sanford: *Clinical Diagnosis and Laboratory Methods*, ed. 9, Philadelphia, 1939, p. 328, W. B. Saunders Co.
26. Wiener, A. S., Cremland, B. H., Hyman, M. A., and Samwick, A. A.: *Am. J. Clin. Path.* **11**: 102, 1940.
27. Wiener, A. S., and Peters, H. R.: *Ann. Int. Med.* **13**: 2306, 1940.

4500 OLIVE STREET

Ernst, S.: Contribution to the Pathology of Arcuate and Bicornate Uterus,
Zentralbl. f. Gynäk. **65**: 551, 1941.

The author reviews the literature on pregnancy in the abnormally formed uterus and presents a detailed study of 19 such cases. He finds that exclusive of unfavorable position, poor contractions, and early separation of placenta there may be expected with great regularity many unusual conditions affecting the fetus, such as amputations and developmental defects as well as all possible malformations of the placenta. The peculiarities of placentation are attributed to faulty implantation. Hyperemesis or pre-eclampsia often occurs. The increased incidence of toxic conditions in association with uterine anomalies is attributed to a more or less generalized constitutional weakness of the pregnant woman.

R. J. WEISSMAN.

POSTOPERATIVE HORMONAL THERAPY TO SPARE REMAINING OVARIAN TISSUE*

W. DUNCAN OWENS, M.D., MIAMI BEACH, FLA.

IT HAS always been, and still is, my practice to treat ovarian tissue in a conservative manner when possible. There has never been, however, any hesitation at sacrificing an ovary, the adequacy of whose blood supply I questioned in the least.

In 1932 I realized with concern and dismay that in an appreciable and increasing number of young women it had been necessary for me to remove their remaining ovarian tissue. Since that time, accurate records have been kept of all such cases that came under my care. Included in each record is a follow-up for not less than six months in all cases and for years in many cases.

During the year 1932 pathology was encountered in 7 women which required excision of one ovary with or without some procedure, such as resection, enucleation of a single cyst or puncture of multiple cysts on the other ovary. Subsequently 3, or 40 per cent, of these women required, because of acute and incapacitating pain, removal of all remaining ovarian tissue at a second operation. In each instance, at the first operation, one ovary had been excised and the other resected and sutured with plain catgut. Within that same year 6 women who had been operated upon by others, lost, in my hands, their remaining ovarian tissue. The record in each of these cases was obtained and carefully studied. In all of them, one ovary had been removed and the other ovary had, no procedure in 1 case, puncture for multiple cysts in 1, enucleation of a single cyst in 1, and resection and continuous suture with catgut in 3.

The procedure applied to the ovarian tissue allowed to remain at the first operation must have been faulty, not only in my hands but in the hands of others. Since in all 3 of my cases and in 3, or one-half, of the others, the resected ovary had been sutured with catgut, it was decided to abandon that procedure in favor of enucleation or multiple puncture whenever possible. When necessary to resect, bleeding points would be tied individually.

In 1933, of 9 women from whom one ovary was removed, some procedure was necessary upon the other ovary in only 7. But subsequently of these 9 women 3 required a second operation for removal of remaining ovarian tissue. In 1 of them nothing had been done to the second ovary while of the others 1 had been subjected only to multiple puncture and 1 had been resected and individual bleeders tied with catgut. During this year, it was necessary to remove remaining ovarian tissue from 8 women

*Read at the Forty-First Annual Meeting of the Chattahoochee Valley Medical Association, Jacksonville, Fla., Aug. 1, 1941.

whose initial operation had been done by others. In all of these one ovary had been removed and the other had, no procedure in 2 cases, multiple puncture in 3, and resection with continuous suture in 3.

There still seemed to be some fault in the technique. It was decided to try a careful decortication with control of bleeding by pressure from hot packs and only to resort to any other procedure when absolutely necessary.

In 1934, of 10 women who lost one ovary, the above procedure was done upon the other ovary in 7 instances, no procedure in 2, and resection with individual ties in 1. Of these 10 cases, 3 came to subsequent removal of remaining ovarian tissue: at first operation 1 had no procedure, while 2 had been decorticated. During this year remaining ovarian tissue was removed from 6 women whose first operation had been done by others. In 1 of these, both ovaries had been resected and continuously sutured, while in the other 5, one ovary had been removed, and the others had, no procedure in 2 cases, multiple puncture in 1, and resection with continuous suture in 2.

Changing of technique had resulted in only a 10 per cent decrease of an altogether too high percentage of patients requiring removal of remaining ovarian tissue. In 9 of 26, or 35 per cent, of my cases and in 20 cases of others this had been necessary. In 7, or 25 per cent, of these 29 cases, nothing had been done to the second ovary and in the 2 cases in my series certainly, and presumably in the other 5 cases also, the blood supply to the ovary had not been knowingly interfered with. Careful study of the history of these 29 cases, all between 19 and 36 years, revealed the following interesting facts:

1. In all cases symptoms of increasing-in-size masses, ranging from local discomfort and a sense of heaviness to a dull ache to actual pain, first appeared in from four weeks to not longer than five months after their first operation, and became severe enough to require operative relief.

2. In none were noted symptoms of hypo-ovarianism.

3. In 20, or 70 per cent, menstruation was as regular as formerly.

4. In 6, or 20 per cent, menstruation was more frequent.

5. In 3, or 10 per cent, menstruation was less frequent.

6. In 17, or 60 per cent, amount or length of flow was unchanged.

7. In 7, or 25 per cent, amount or length of flow was increased.

8. In 5, or 15 per cent, amount or length of flow was decreased.

9. In 3, or 10 per cent, dysmenorrhea was greater than formerly.

10. In 12, or 40 per cent, there was hemorrhage, old or recent, into a simple cyst while 17, or 60 per cent, were simple serous cysts.

It seemed remarkable that these cysts should cause actual pain since simple cysts are not usually painful. Here it is well to recall that all patients developed pain in not more than five months. This rapidity of development, perhaps, accounts for the pain. It also seemed fairly evident that the development of these cysts was not due entirely to scarring of the cortex. It appeared distinctly worthy of note that, although

these cysts developed rapidly, there was little or no suggestion of a deficit of, or interference with, ovarian hormone. It, therefore, was reasonable to assume that the remaining ovarian tissue had taken over all ovarian hormonal duties. It might be argued that these duties had been gradually shifted since one ovary presumably had been fairly slow coming to be of so little value that its removal was indicated. This, however, is not histologically so, because it is a rare ovary that has not some useful areas in it. The sudden operative elimination of even small functioning areas would, thus, cause an immediate burden to be placed upon remaining ovarian tissue. It occurred to me that we might ease down or "spare" this sudden call for an all-out effort on the part of depreciated ovarian tissue by giving a supply of hormone in the form of estrogenic substance. It was and is conceded generally that increased work of a human organ requires greater blood supply than normally. Cyst formation in an ovary whose blood supply has been interfered with is well known and is seen all too often following a salpingectomy. That estrogenic substance might not only supply additional hormone but might also cause increased blood supply to remaining ovarian tissue was hoped on the basis of 2 then recently observed cases. Both of these women had been operated upon elsewhere years previously, losing all of one ovary and a part of the other. Several years had passed for each of them before menopausal symptoms appeared. When menopausal symptoms appeared, they were so severe that it had taken huge doses of estrogenic substance to relieve them, one patient having been given 48,000 units in one week and the other 60,000 units in eight days. Pain, rapidly increasing, and a very tender cystic mass in the pelvis caused me to operate. In each patient was found an ovarian cyst distended with fresh hemorrhage.

Believing that moderate doses of estrogenic substance could, at the very least, do no harm, it was decided that each patient who lost a considerable part of her ovarian tissue should be given estrogenic substance according to the following program: 2,000 units of estrogenic substance in oil to be given intramuscularly at a single dose each week when not menstruating; first dose eight days after operation; postmenstrual dose five days after cessation of flow. Because, in the 29 cases studied, symptoms began invariably within the first five postoperative months this program was to be continued for six months postoperatively. Each patient falling into this group has had a minimum of postoperative pelvic examination at about six weeks, about three months, about six months, and about every six months thereafter when feasible. Those in whom any pathology was found were examined more frequently, immediately premenstrually, immediately postmenstrually, and intermenstrually.

This report includes all cases from January, 1935, through December, 1940, with follow-ups through June, 1941, a total of 57 women, varying in age from 18 to 34 years, whose pathology required removal of a part of their ovarian tissue. To state it in other words, all these 57 women retained part, but not all of their ovarian tissue. When the blood supply

to an ovary was questionable that ovary was removed. Procedures followed upon remaining ovarian tissue were: 44 decortications, 7 enucleations of single cysts, 5 multiple punctures, 18 resections with interrupted suture or with individual ties of bleeding points; a total of 74 procedures in 57 patients. This discrepancy is accounted for by the fact that, in 17 instances, only a part of both ovaries was removed but that part always equalled at least half of the ovarian tissue.

In only 2, or 3½ per cent, of these 57 women was postoperative pathology found. Neither of them has required operation. In a 19-year-old girl with pelvic inflammatory disease, somewhat more than one-half of each ovary was resected and bleeders tied individually; both tubes and appendix were also removed. Twenty-nine days postoperatively, at what proved to be three days premenstrually, she complained of pain in the left lower quadrant of the abdomen radiating to the back and rectum. This pain was described as a severe ache, continuous and without nausea. Pelvic examination the same day disclosed only a tender mass, 4 cm. in diameter, lying quite low in the left adnexal region but not in the cul-de-sac. She had received 3 doses of 2,000 units of estrogenic substance; the next dose was due the same day and was given. This patient has been carefully watched during the ensuing four years and in June, 1941, the mass was no larger and she has been symptom-free for more than three years. Menstrual periods have occurred regularly at twenty-eight-day intervals and have been painless and unremarkable. Estrogenic substance was given to her according to schedule until all pain ceased, at the end of eight months, when it was discontinued. Perhaps larger amounts immediately postoperatively might have prevented the formation of this cyst. The other case was a 31-year-old woman from whom one multiple cystic ovary was removed three years ago, at the time of a total hysterectomy; the other ovary which was sclerocystic was decorticated. Three months postoperatively she complained of a heaviness and aching in the right side of the pelvis. She had received estrogenic substance as planned. At examination only a tender mass, about 5 cm. in diameter, was found in the right side of the pelvis. Her pain ceased after seven months during which time she received estrogenic substance routinely. She still has a cystic mass, perhaps slightly smaller than originally, but remains entirely free from pain.

During this six-year-period 47 women from whom others had removed part of their ovarian tissue have been seen. Of these, only 28, or 60 per cent, required removal of their remaining ovarian tissue. The other 19, or 40 per cent, presented themselves early upon the development of postoperative discomfort or pain and were treated with estrogenic substance according to our routine except that in 6 cases the first 4 doses were of 10,000 units weekly. They have been carefully followed. Increase in size of mass ceased almost at once while pain and discomfort ceased in never longer than nine months. None of these 47 women had received estrogenic substance before consulting me.

DISCUSSION

Greenhill¹ states that "Conservative surgery of the ovaries should be reserved for only a certain proportion of women under 40 years of age." When he states, "In young women it is far better to risk the necessity of another operation a few years later" he implies that such

necessity is not infrequent. He² again states, “. . . . an ovary should not be removed unless it is absolutely necessary, especially in a young woman. One can never tell when the remaining ovary may have to be removed” Runge³ found a 15.5 per cent incidence of cystic ovaries in 196 traced women of 345 from whom one ovary had been removed. If the remaining ovary was subjected to no procedure, and no mention is made of such procedure, his figure is lower than my 25 per cent in 29 cases, but still high. Other statistics of the incidence of cyst formation in remaining ovarian tissue have not been found.

The incidence of 35 per cent in my present series of 26 cases, 1932 through 1934, under various types of operative technique, may seem high but, perhaps, other analyses might find it just as high or even higher.

SUMMARY

1. From 1932 through 1934 varied operative technique was employed in conservative ovarian surgery.

2. Changing technique resulted in only a small decrease in the incidence of rapid and painful cystic formation in remaining ovarian tissue.

3. During this three-year period, 9 of 26, or 35 per cent, of my cases required secondary operative removal of all remaining ovarian tissue. This was also necessary in 20 other cases.

4. In the six-year period, 1935 through 1940, with follow-ups through June, 1941, of 57 women who lost a part of their ovarian tissue none has required subsequent operation and only 2 have shown evidence of pathology of remaining ovarian tissue. This result is attributed to the routine postoperative use of estrogenic substance as described. This assumption is further borne out by the fact that operation has been avoided in 40 per cent of other women who presented themselves with discomfort or pain from early postoperative cystic formation.

REFERENCES

1. Greenhill, J. P.: Ed. Note 1934 Year Book of Obstetrics and Gynecology, p. 443.
2. Greenhill, J. P.: Ed. Note 1936 Year Book of Obstetrics and Gynecology, p. 543.
3. Runge, H.: *Monatschr. f. Geburtsch. u. Gynäk.* 100: 233, 1935.

Fox, Frances Hill: *A Comparison of the Irving and Pomeroy Methods of Tubal Sterilization*, Surg., Gynec. & Obst. 71: 462, 1940.

Of 432 operations on the Fallopian tubes for the purpose of sterilization, there were no failures by the Irving technique; of 50 cases there was one failure by the Pomeroy technique.

WILLIAM C. HENSKE.

THE USE OF STILBESTROL IN THE MANAGEMENT OF THE MENOPAUSE

Z. J. R. HOLLENBECK, M.D., AND P. J. REEL, M.D., COLUMBUS, O.

(From The Department of Gynecology and The Gynecological Endocrine Clinic, College of Medicine, The Ohio State University)

SINCE the introduction of stilbestrol,* there have been many somewhat conflicting reports on its toxicity and the clinical response to its use. Nausea, as a sign of possible toxicity, has been reported variously as occurring in from none to 80 per cent of the cases treated, and vomiting in from none to 32 per cent of the cases.¹ In the management of the menopause, investigators have almost invariably reported a certain number of cases in which they were unable to relieve the symptoms with stilbestrol. The findings in the treatment of this group of patients are not in accord with many of these reports.

MATERIAL AND METHOD

Our series represents 119 cases, of which 101 were at or beyond the menopause and 18 were younger women with a diagnosis of hypovarianism. Of the 101 patients in the menopause group, 67 were natural and the remaining 34 had a menopause induced by surgery or radiation. The 18 younger women included 11 cases which presented either continuously or cyclically, mild to moderately severe symptoms of secondary ovarian failure. These cases are included with the menopause group, bringing this to a total of 112.

The clinical response in all patients treated was correlated with the systemic estrogenic response as revealed by the vaginal smear. An "adequate response" to therapy, as reflected in the vaginal smear, was sufficient to produce an absence of deep "atrophy" cells with very small nuclei, a marked diminution in the number of leucocytes and a preponderance of cornified epithelial elements. The smears were interpreted by the pathologist who was not aware of the identity of the patient or the status of therapy. Some patients received only oral medication, others received the drug intramuscularly and still others by both routes, either singly or concurrently. The dosage of stilbestrol varied in the oral therapy from 0.05 mg. to 2 mg. daily and in the parenteral therapy from 0.1 mg. to 15 mg. per week. The duration of treatment was from two weeks to ten months.

*The stilbestrol used in this study was furnished through the kindness of The Department of Medical Research, The Winthrop Chemical Company, Inc.

MENOPAUSE

This group of patients presented the typical menopause syndrome of hot or cold flushes, headaches, nervousness, dizziness, emotional instability, insomnia, and various vague aches and pains. In addition to these symptoms, 9 patients complained also of pruritus and dyspareunia which was associated with a senile vaginitis. Several of this group of patients had an associated hypertrophic arthritis which had responded favorably to previous natural estrogen therapy. One patient, with an involutional melancholia, who had not responded to as much as 100,000 I.U. of estrone each week, was well controlled with 1.5 mg. of stilbestrol by mouth daily.

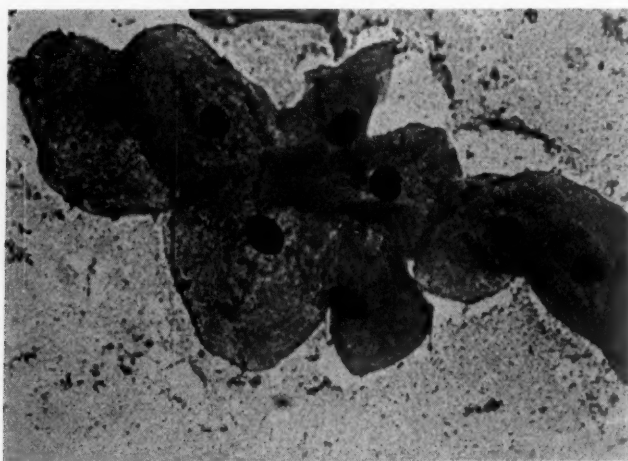


Fig. 1.—Photomicrograph (high power) of a typical menopausal vaginal smear, showing the oval squamous epithelial cells with large nuclei and many polymorphonuclear leucocytes. This smear was made from a woman who presented typical menopausal symptoms.

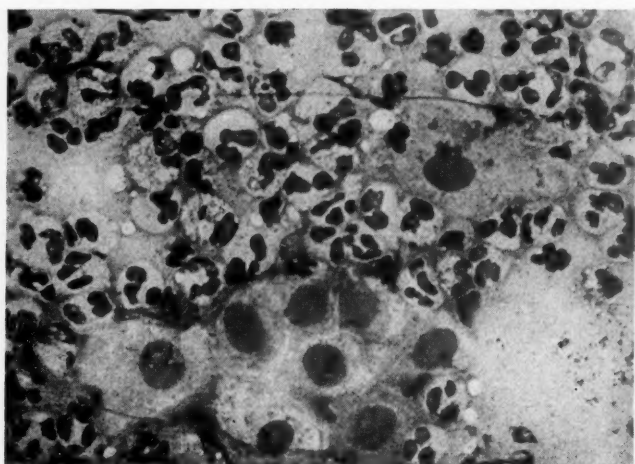


Fig. 2.—Smear from the same patient after relief of symptoms with stilbestrol therapy showing an adequate response. Note the absence of leucocytes and the cornification of the squamous cells.

The results in the group of menopausal patients can be briefly stated. In no case in which there was an adequate response in the vaginal smear was there failure to relieve the patient.

MISCELLANEOUS

This group included three young patients with a secondary amenorrhea which probably represented, in each case, a premature ovarian failure. These patients had failed to respond to pituitary gonadotropic hormone and thyroid therapy. Stilbestrol was used merely to produce estrogen withdrawal bleeding. This was accomplished several times in each case with oral doses varying from 1 to 2 mg. daily, for a period of from three to six weeks. These patients all noted a feeling of well being for the duration of stilbestrol therapy.

One patient presented herself with a history and physical findings of a functional menstrual irregularity. She was flowing profusely at the time of her visit. In an effort to stop the bleeding, she was given 1 mg. of stilbestrol intramuscularly and 1 mg. orally for six days. She reported that the bleeding stopped after 3 oral doses and that she had no further bleeding for eleven days. She did not return again to the clinic.

One patient complained of severe headache associated with her menstrual periods. During one menstrual cycle she was given 1 mg. of stilbestrol intramuscularly twice each week. She noted no improvement.

Two cases of primary amenorrhea in women, aged 23 and 21 years, were studied. Both patients presented, on pelvic examination, an infantile cervicouterine ratio, and biopsy revealed an atrophic endometrium. These patients were treated for seventeen and thirteen months, respectively. The endometria of both patients showed marked estrogenic response and the uteri approached adult size. The first patient menstruated 9 times without withdrawal of stilbestrol, and the second patient menstruated only 3 times, once apparently spontaneously and twice only after stopping the medication. The dose of stilbestrol in these cases was 1 mg. twice weekly, parenterally, and 1 mg. daily by mouth, respectively.

The last patient in this group was treated with large doses of stilbestrol, as Lissner² has suggested, in an attempt to influence a marked, unexplained virilism. She received, within a period of 110 days, 158 mg. intramuscularly and 41 mg. by mouth. No change was noted in her hypertrichosis, but there was considerable enlargement of the breasts; and the endometrium and vaginal mucosa showed a marked estrogenic response.

SIDE EFFECTS

Nausea occurred in 23 patients. Three of these patients also vomited. Six patients seemed to develop a tolerance to the drug, and as therapy was continued the undesirable effects disappeared. In some of these, the dose of the drug was decreased for a few days and then restored to its original amount. Nausea or nausea and vomiting were severe enough to demand discontinuance of therapy in 7 cases, or 5.9 per cent.

Postmenopausal uterine bleeding occurred during treatment in two cases. This was not troublesome, because it was possible to adjust the dosage so that no bleeding occurred and yet the symptoms were relieved.

No other undesirable or toxic effects were noted.

CONCLUSIONS

The estrogenic effect of stilbestrol is similar to estrone.

The indications for the use of stilbestrol are the same as for estrone.

Nausea and vomiting are apparently an individual idiosyncrasy. Some patients evidently develop a tolerance to this effect.

The optimum dose is from 0.5 to 1 mg. by mouth daily and 1 mg. intramuscularly.

Stilbestrol should be used only at the direction of a physician.

REFERENCES

1. Morrell, J. A.: *J. Clin. Endocrinology* 1: 419, 1941.
2. Lissner, H.: *Endocrinology* 27: 385, 1940.

Seimeanu, A., and Adamesteanu, C.: **The Pathogenesis of Perineal Pruritus and Its Treatment by Epidural Injections of Magnesium Sulphate**, *Presse méd.* 47: 1498, 1939.

Within four and a half years the authors saw 51 cases of idiopathic perineal pruritus in 65,000 gynecologic consultations at a Hospital in Bucharest. Cases of pruritus of a known etiology are not included.

Previously the authors had used local medications, autohemotherapy and physiotherapy. In this series all rebellious cases of idiopathic perineal pruritus were treated solely with epidural injections of 20 per cent magnesium sulfate.

The writers maintain that perineal pruritus is a syndrome capable of being induced by a number of factors (endogenous and exogenous intoxications and endocrine disturbances) acting upon the sympathetic nervous system in general but chiefly involving the sacral sympathetics. These irritative factors produce an imbalanced and sensitive sympathetic system, localized by an altered psyche to the perineo-genital zone, normally the location of voluptuous sensations. The psyche of the affected individual becomes aware of the increased voluptuous sensations which are then interpreted as a pruritus.

The centripetal path of perineogenital sensation is the sacral sympathetics which probably exhibit a biochemic imbalance in their structure, characterized by a decrease in the magnesium ion.

The writers inject 5 to 6 c.c. of freshly prepared, sterile, 20 per cent solution of magnesium sulfate into the epidural space, using the Cathelin technique. The patient remains on the table for fifteen minutes after the injection. The injection is repeated every third day for a total of 4 to 5 times in the majority of cases. A few cases required as many as 8 to 9 treatments.

The results are listed as follows: failure in 5 cases; 10 other cases had been observed less than six months and are not included in the final figures; in 36 other cases, observed six months to five years, 13 per cent evidenced mild recurrences at time of menses or following the use of coffee, while 87 per cent remained free of their perineal discomfort.

CLAIR E. FOLSOME.

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

MENTAL DISORDERS ASSOCIATED WITH CHILDBEARING

DAVID A. BOYD, JR., M.D., INDIANAPOLIS, IND.

(From the Department of Neurology and Psychiatry, Indiana University School of Medicine)

(Continued from page 163, January issue.)

PSYCHOPATHIC PERSONALITY (WITH AND WITHOUT PSYCHOSIS)

Psychiatric classifications contain an ill-defined group termed "psychopathic personality" (older term "constitutional psychopathic inferiority") which embraces a host of personality deviations. Ordinarily, these individuals are not actually psychotic but the warping of their personality and difficulties in adjustment are so severe as to warrant classification as abnormal individuals. In this group have been placed those individuals whose unstable, erratic, and impulsive behavior, emotional instability and antisocial attitudes bring them into conflict with established law and order. Some believe that the personality and emotional deficiencies are constitutionally determined; others maintain that unfavorable and emotionally warping influences in early years are the most important etiologic factors. Whatever the cause may be, the final personality pattern is unwholesome and poorly designed for social adjustment. Among the outstanding features of this personality pattern are selfish egocentricity, untruthfulness, disregard of the rights and opinions of others, cruelty, extreme self-assertion associated with a complete lack of foresight or ability to profit by past experience. Often these individuals are of normal or above average intelligence but still are unable to control their instinctive, impulsive behavior.

The defects of this personality pattern are usually manifested in childhood or adolescence but sometimes do not become fully apparent until early maturity when the individual is emancipated from parental dominance and protection. Often their limited capacity for adjustment does not become apparent until the increasing social and vocational demands of early adult years exceeds their meager adaptability. When this occurs, the individual responds with violent, antisocial, selfish, and cruel reactions instead of utilizing more socially acceptable and mature methods. Pregnancy and the responsibilities of parenthood may supply just this test of personality adequacy. In addition, sexual precocity and indulgence are frequently noted in this personality type and extramarital pregnancy is of common occurrence. When these individuals become pregnant, either maritally or extramaritally, their behavior is

marked by the same impulsive and egocentric trends which have been demonstrated throughout their earlier years. Occasionally, the novelty of the first pregnancy may be sufficient to inhibit their instability temporarily but later gestations will disclose their psychopathic personality organization. In response to severe strains such as pregnancy, these vulnerable personalities may break over into short, atypical psychoses which fade out, leaving the unwholesome character pattern as a residual. For these individuals, pregnancy is another difficult life situation to which they react in their customary manner.

CASE 5.—A single woman, aged 24 years, gravida i, was admitted to a home for indigents because of inability to work due to her pregnancy. Physical examination revealed a normal pregnancy in the sixth month without evidence of associated organic disorder. However, her conduct led to serious doubts regarding her sanity. She was extremely sensitive, easily irritated, and had temper tantrums without apparent provocation. At times she became unmanageable, showing a violent response to simple situations which could not be reasonably a cause of irritation. She maintained that the matron persecuted her and made life miserable and she resented everyone. For example, she became irritable when her room was not cleaned in the manner she desired and struck her roommate across the mouth although this girl was not bothering her. Her behavior at the dining table caused apprehension among her fellow lodgers because of her violent spasms of rage and recrimination, maintaining that they sucked their teeth and talked of their diseases and operations for the sole purpose of increasing her nausea of pregnancy. It was necessary to give her a single room and allow her to eat alone because of her surliness. When another resident admired her pretty clothes, she became incensed because she believed that these remarks of admiration were an insinuation that she was a prostitute "who had some rich, gray-haired old guy buying her clothes." She locked herself in the bathroom and occupied herself with sewing, regardless of the inconvenience to others. When asked to leave the bathroom, she threatened to stab the matron with scissors if she were touched. These are only a few examples of the irritability, sensitivity, and explosiveness displayed by this patient.

The history revealed that the above behavior was a continuation of her lifelong pattern. She was born in the South of a schizophrenic mother and shiftless, unstable father, and she learned early to respond to any untoward situation by antipathy and violence. When the patient was 10 years of age, the mother was sent to a mental hospital and the child regarded this with equanimity for "my mother always hated me because my father loved me so much and was willing to do anything for me." At 12 years of age, she was placed in an orphanage for "my stepmother hated me because she was jealous of me," but other information reveals that she was incorrigible, had temper tantrums and irritable outbursts and would not account for her nightly absences from home. At 14 years of age, she was sent to the home of an uncle and her temper tantrums and erratic behavior soon caused a marital separation "because he liked me so much that my aunt was jealous and hated me." She then secured work as a housemaid, usually being discharged from her position after one or two days. If the employer made suggestions or criticized her, she became enraged, even quarreling with small children. She was frequently admitted to indigent homes because of inability to hold a job. Between the ages of 19 and 24 years, she was admitted to hospitals at least five times for vague complaints and illnesses for which no organic basis could be found. It is not known when her sexual promiscuity began. When she learned of her pregnancy she had a violent temper storm and drove her paramour away because he was a shiftless drunkard.

Delivery was uneventful but the patient soon became difficult to manage. She talked sentimentally of the baby's need for a mother and how beautifully she would clothe her. A moment later she would speak of her intention to become an opera star or a fashionable mannequin or to enter some other type of work which was obviously far beyond her abilities. She enjoyed making sarcastic, cutting remarks about other patients, called them foul names and incited one against the other so

that she might enjoy the quarreling that ensued. She maintained that she was only an average girl and had no idea why everyone was so "mean" to her. According to the patient, her difficulties in adjustment were wholly on the basis of "meanness and silliness" of all the other people in the world. A diagnosis was made of: Psychopathic personality; unstable, explosive, antisocial type.

It is obvious that these women are incapable of wholesome motherhood. Often they vent their hostility on the newborn child by rejection, inattention to its needs, or even by slapping and cursing the infant because it represents an obligation and responsibility. Treatment of these patients is ineffectual and punishment does not act as a deterrent.

PSYCHONEUROSES

The psychoneuroses resemble the psychoses in that they represent symbolic physical and mental expressions of underlying emotional problems. They differ, however, in that they do not include a definite break with reality; the patient realizes that the disorder is in himself although he may erroneously believe the difficulty to be physical in nature and finally, although the sufferer may be incapacitated, he still remains a socially organized individual. The symptoms of the neurosis have their genesis in some emotional dilemma in which the individual is urged on by powerful instinctive, pleasure-seeking, selfish motivations and yet held back by moral and ethical obligations. Pregnancy and motherhood with all their inconveniences, responsibilities, and demands for unselfishness are times of great vulnerability, especially for individuals already possessing a neurotic constitution.

The focal beginning of all neuroses is a state of anxiety; the precise type of neurosis depends on how the individual handles this anxiety. It may remain as a relatively pure "anxiety state" with such mental symptoms as apprehensiveness, states of panic or phobias such as fear of death, insanity, or impending catastrophe. Physical manifestations such as tachycardia, nausea, diarrhea, dyspnea, or dizziness are usually noted. Other patients will achieve mental peace by converting this anxiety into physical symptoms, such as anesthetics, paralyses, blindness, convulsions, etc., and this syndrome is designated "conversion hysteria." Still others will avoid the basic emotional conflict by obsessively contemplating a substitute idea which is painful but not so distressing or disorganizing as the original problem, or find relief by carrying out some compulsive ritual; this reaction pattern is termed "obsessive-compulsive neurosis."

In the present series of cases the best single index of neurotic diathesis was the prepuerperal personality of the patient. Nearly every one had a history of lifelong neurotic traits. Some were weak, clinging, inadequate individuals who always became disorganized when confronted with a difficult situation. Others were selfish, whining, querulous types who had temper tantrums whenever frustration appeared imminent. Still others were timid, apprehensive persons who had always been unusually concerned with their physical, mental, or moral health.

The neurotic patients in this series could be classified grossly in three groups if precise psychiatric diagnoses were disregarded and the cases studied from the standpoint of the genesis and form of their reaction pattern. In one group the neurosis appeared to be a natural outgrowth of the patient's personality deficiencies. These individuals were of a selfish, irritable, unstable type who were usually sexually and emotion-

ally maladjusted in their marriage. The neurotic symptoms appeared after the first delivery which was neither complicated nor unusual. These patients were never well thereafter, becoming irritable, petulant women with innumerable pains and a host of visceral disturbances. Usually there were episodes of extreme anxiety with fears of impending death, prolonged bouts of weeping and self-pity and disinterest in the home and children because of pathologic preoccupation with their own symptoms. Each ensuing pregnancy added an increment to the symptoms until a pattern of chronic neurotic invalidism was established.

CASE 6.—A married woman, aged 24 years, para ii, was admitted to the hospital six weeks after her second delivery. She had remained in bed since this delivery, wept frequently, had episodes of irritability, and complained of pain in nearly every part of the body.

Physical examination revealed a well-developed, well-nourished woman. There was no evidence of physical disorder and laboratory studies were negative. The patient was apprehensive and tense and made a constant effort to win the sympathy of the physicians and nurses. She complained of palpitation, numbness of the arms and legs, and pain in the back. Frequently she berated her husband, stating that he should not have allowed her to become pregnant, that he was not attentive enough, and that he preferred to be with other people rather than to attend to her needs. At times she feared that she had some incurable physical disease and at other times had a phobia of oncoming insanity. There were many episodes of self-pity and weeping associated with a repetitious enumeration of her many symptoms. She found many excuses for her own shortcomings, stating that the second pregnancy was "just too much for me" and "I should never have been allowed to become pregnant with my womb in such bad condition." When her attention was momentarily diverted by some entertaining event, she became interested, vivacious and friendly but relapsed a few moments later into her weeping, complaining behavior pattern. A diagnosis was made of: Psychoneurosis; anxiety hysteria.

The family history was negative for any mental abnormality. The patient was the youngest of eleven siblings and was petted and waited upon as the baby of the family. The menarche occurred at 12 years of age; the menstrual periods were painful and associated with nervousness and irritability. She completed high school, was a popular girl, and always had many friends. At home she was dictatorial, disliked anyone who disagreed with her, and was always dissatisfied although she was given luxuries beyond the family means. She loved to dance, to attend social functions, and to be entertained and demanded expensive, fashionable clothing. Whenever her wishes were not immediately granted, she had a bout of weeping and depression or else became disagreeable and sarcastic. After completing school she worked as a clerk for a short time but left this work to remain at home where others would wait upon her.

She married at the age of 21 years to a steady, dependable man who gave her everything possible within the limited means of his small salary. The first pregnancy occurred shortly after marriage and her health was excellent throughout gestation. The delivery was difficult and required instrumental assistance. Her postpuerperal convalescence was very slow, and she had many complaints with no apparent organic basis.

The second impregnation occurred two years later and was contrary to the patient's wishes. As soon as she learned of the pregnancy she became apprehensive and irritable and complained of pelvic pain, faintness, dizziness, and palpitation of the heart. After the second delivery, which was easy and uneventful, her symptoms became innumerable. She refused to leave her bed, was careless and disheveled in appearance, and wept when confronted with any household task. It became necessary to send the children to the grandparents because of her neglect and disinterest, and the husband had to do the housework and cooking. She complained constantly of her symptoms and became indignant if the family would not listen and accused them of callousness, sobbing that they had never done anything for her. Episodes of

uncontrolled laughing and weeping occurred. Numerous physicians were in attendance, the patient discharging each one as soon as he suggested that she had no physical disorder and should resume her domestic duties.

In the hospital the patient was unable to sleep and complained constantly. With psychotherapy she slowly gained insight into her selfishness and the defensive aspects of her illness. She soon was able to face the fact that her illness was not physical in origin but was really an effort to avoid the monotony and responsibility of an adult maternal routine. She was discharged after one month of hospital residence. Three years later the husband wrote that his wife was "a changed woman—perfectly healthy and interested in her home and children."

The second group included those individuals of an unstable personality who were able to make a fair life adjustment until confronted with some puerperal problem or conflict with which they were unable to cope. In this group were such cases as hysterical convulsions and chorea in a timid, dull single girl who found herself pregnant, and prolonged hysterical stupor in an unmarried woman after several bungling, painful attempts at abortion. The following case illustrates the development of such a syndrome:

CASE 7.—A married woman, aged 20 years, para i, gravida iii, was admitted to the obstetric ward because of pain in the right lower quadrant of the abdomen, nausea, chills, and sweating. These symptoms began on the day of admission but the patient had been "nervous" throughout gestation. The first pregnancy terminated in a normal delivery; the second ended with miscarriage at three months.

Physical examination disclosed a well-developed, well-nourished woman who was not acutely ill but whose facial expression indicated great pain. The blood pressure was 115/80. Further examination was negative except for pregnancy nearly at term. Urine examination revealed a trace of albumin and numerous white blood cells but other laboratory studies were negative.

On the second day after admission, the patient had a convulsive seizure with twitching of the mouth and dorsiflexion of the head and spine. This attack was synchronous with the onset of labor. Six hours later there was another convulsion of five minutes' duration, the patient assuming the opisthotonos position. After one minute of relaxation, a similar seizure occurred lasting seven minutes. During these attacks there was marked respiratory embarrassment and cyanosis. A short time later the uterine contractions ceased and no further convulsions occurred. Repeated examinations failed to reveal any evidence of a toxemia of pregnancy.

Psychiatric examination revealed a cheerful young woman who appeared to be in good physical condition. She was not very intelligent and her reactions suggested that she came from a low socioeconomic and cultural group. The patient had been reared in a small town in a strict, religious environment and was taught that sexual transgression was the greatest possible sin. At the age of 17 years she had a sexual relationship (the patient stated that she had been raped) and soon discovered that she was pregnant. The father of the child treated the matter as a joke, told everyone about it and finally decamped, leaving her the object of scorn and ridicule throughout the community. When she informed her father of the pregnancy, he ordered her from the home. She went to another town, in a state of anxiety and tension, and entered a hospital for delivery, telling numerous protective falsehoods. The delivery was uncomplicated, but the child was deformed, having a myeloencephalocele, spina bifida and talipes. She regarded this as God's punishment for her sins. After discharge from the hospital she was desperate, fearing to return home with a sick, deformed child. She left the child on a doorstep, excusing herself by thinking that it would get more medical attention in this way. The baby was traced to her by the footprints and a greater scandal occurred, and she was brought to trial for child neglect and desertion. Although acquitted by a kindly judge who felt that she had already suffered enough, her unpopularity in the community only increased. The child was a constant care but its death at six months seemed to

her to be the final payment for her sin and guilt. She became highly hysterical, fainted many times, and "jerked all over."

A short time later she married and, although she loved her husband, she was sexually frigid. She became an invalid and each time she saw a picture of the dead child she fainted or had screaming spells, usually being ill for several days. There seemed to be no way of reaching peace and happiness at home, and she could gain relief from her feelings of guilt only by going to church and praying for hours for forgiveness and another child. These reactions were intensified when her second pregnancy ended by miscarriage.

During the present gestation she was obsessed by a constant fear that God would punish her by great pain or even death. In addition, there was a tremendous fear that this child would be malformed as her culminating punishment. When she came to the hospital she was uncomfortable and frightened because of cystitis of moderate severity. With the onset of labor, her underlying anxieties became unbearable. She stated that she became overwhelmed when these intolerable feelings of tension and fear reached a certain intensity and these emotions were then transformed into a convulsive seizure.

Psychotherapy of an explanatory and reassuring type produced a rapid and satisfactory improvement. After unburdening herself of her fears and feelings of guilt, she was able to look forward to delivery with confidence and tranquillity. No further abnormal behavior occurred, and she was discharged from the hospital after five days of residence. She delivered a healthy child at home and was apparently a cooperative patient except for one or two "slight spells of nervousness." Her postpartum course was uneventful except for recurrent pyelitis but no further neurotic manifestations occurred. A diagnosis was made of: Psychoneurosis; conversion hysteria.

This group also included women who were confronted with a difficult economic situation complicated further by repeated pregnancies. After seven or eight pregnancies their physical reserve was depleted, their socioeconomic status precarious and their life one of drudgery and constant attendance to an ever-increasing family. Another pregnancy served as the final straw, the patient developing a psychoneurotic illness in the face of this intolerable situation.

The third group included highly complex neuroses which were the expression of deep emotional conflicts and attitudes of guilt due to the sexual aspects of the pregnancy. The physical and physiologic disturbances of gestation appeared to play no role in the genesis of the syndrome. Rather, the conception and delivery of the child seemed to have a deep psychologic significance and revived latent conflicts and problems which usually were concerned with sexual sin, guilt, and distorted emotional attitudes of childhood years.

CASE 8.—A married woman, aged 29 years, para ii, was admitted to the hospital one month after the second delivery because of suicidal gestures and two murderous assaults upon her son, aged 4 years. The last delivery, occurring in the seventh month of gestation, was uncomplicated and the hospital course was uneventful. The infant died after one day. While in the obstetric ward, the patient appeared depressed, refused her medications, and insisted on leaving on her ninth day. She remained in bed at home for two weeks and often spoke vaguely about the authorities coming for her. The episodes of weeping became more frequent, and she blamed herself constantly, stating that she had caused the miscarriage by overwork. In the next few days she refused to eat, had persistent insomnia, and cut up ropes with which to hang herself, although she made no actual attempts. On one occasion she locked herself in the bathroom and threatened to drink poison; once she stood before her husband and drew a cord tightly about her neck but released it when she be-

gan to strangle. Shortly before admission she suddenly assaulted her son and the next day she again strangled him, the child being cyanotic and limp when the husband intervened.

Physical examination revealed a well-nourished, stocky woman who was in excellent physical condition. Neurologic and laboratory studies were completely negative. The patient was shy, embarrassed, and somewhat depressed. She stated that she had lost all interest in life and everything seemed different and without meaning. Her greatest concern was the fear that ideas might come to her to harm someone and that she might carry out these impulses. When she thought of the possibility of inflicting some cruel injury upon others, she became terrified. These obsessive thoughts recurred constantly and caused her much anguish, the patient stating, "Doctor, my heart must be just full of murder." She was afraid to return home lest she carry out these sadistic, compulsive urges. A diagnosis was made of: Psychoneurosis; obsessive-compulsive neurosis with secondary depression reactions.

The family history was negative for mental abnormality. The family were a lower class English group and had spent much time "on the Dole." The father was a strong-minded, domineering individual who taught the patient to repress sternly her own emotions and personality and accept whatever treatment her superiors dispensed. She spent much of her girlhood "in service," was mistreated and abused but learned to accept it with docility although she inwardly raged. Her sexual interests were early aroused but were rigidly repressed because she believed them to be sinful. All these factors contrived to make her timid, fearful, self-effacing, over-conscientious, and meticulous. At 17 years of age she was seduced or raped by the husband of her mistress. She was extremely frightened and felt guilty but was incapable of defending herself and was afraid to tell her rigidly moral family. After repeated relationships she became pregnant and the employer forced her to have a criminal abortion. She became seriously ill, had a fever of 104° F., and was constantly obsessed by the thought: "I've murdered a child." Later her employer resumed the relationships and she often thought of committing suicide because, while she resented his assaults, she was too timid to defend herself or to expose his behavior.

At the age of 20 years, she married a stable, devoted man. He found her to be sensitive, easily hurt, anxious, and always requiring encouragement and reassurance. Her first pregnancy and delivery were uneventful. A few weeks after delivery the thought suddenly came to her: "I might murder this baby." She became frightened that she might have the impulse to strangle him and was afraid to be alone with the child. She spent her days on the streets with the infant in his carriage so that passers-by could stop her if she made a homicidal attempt. To her husband she complained of a choking sensation in the throat and intense nervousness and expressed the fear that she could not "bring up the boy." Several physicians were consulted because of "nervousness" but none ever asked why she was emotionally disturbed and each merely prescribed a mild sedative.

The next pregnancy, four years later, was planned. Severe nausea and vomiting occurred in the third month and she later complained of severe uterine pain and choking. She frequently expressed the fear that she would "lose the baby" before term. When this actually happened in the seventh month, her feelings of guilt and responsibility were severe and painful. The belief that she had killed another baby was distressing, but it was soon replaced by the terrifying obsessive fear that she might strangle her son. Finally, in two periods of mental unclarity, she actually attempted to carry out this compulsion.

Prolonged hospital residence with extensive psychotherapy and convulsive shock treatment produced a satisfactory improvement in this patient. It was felt that she was a vulnerable individual and that further pregnancies might precipitate another severe mental disturbance.

The psychoneuroses associated with childbearing are probably more numerous than our statistical tables would indicate, but the majority

are never seen by psychiatrists. Usually they drift into a chronic neurotic state and present a constant problem to the obstetrician. During gestation they have innumerable complaints and inexplicable symptoms and not infrequently demand therapeutic interruption of the pregnancy. In the state of our present knowledge, such termination is unjustified. It will not cure the neurosis and may even aggravate the neurotic disorder because of associated feelings of guilt and remorse.

The prognosis of the psychoneurotic patient will depend on her personality assets and the psychotherapeutic treatment she receives. A fair number will make a spontaneous social recovery once the strain of pregnancy is removed, but the recovery rate will be materially increased by psychotherapeutic efforts on the part of the physician. Practically all these patients, whether recovered or not, will be able to live in the community, some as chronic neurotic invalids, others as unhappy, physically uncomfortable "nervous" women. The neurosis is liable to return or to be exaggerated by further pregnancies which add to the patient's life burden.

EPILEPSY

Pregnancy may be related to epilepsy and its associated psychoses in two ways. In the first instance, pregnancy may occur in an epileptic patient and may improve, aggravate, or not affect the convulsive disorder, but it is impossible to predict its effect in any given case.¹⁰⁵ The patient with a paroxysmal convulsive disorder, whether pregnant or not, is liable to episodic mental disturbances, such as psychic equivalents, postconvulsive confusional states, etc. Occasionally, these mental disorders occur in the pregnant epileptic patient, but the psychosis is due to the paroxysmal convulsive disorder, not to the pregnancy which acts only as an aggravating factor.

The second possible relationship between these two disorders is when the initial convulsion occurs during pregnancy, marking the beginning of an epileptic syndrome. The convulsive disorder then runs its own course, sometimes marked by psychotic episodes and eventuating in intellectual and personality deterioration. Again, the mental disorder is a part of the convulsive syndrome, the pregnancy serving only as the precipitating factor. In both instances, it would be incorrect to ascribe any specific effect to the gestation inasmuch as all these mental disturbances are seen both in epileptic men and in women with convulsive disorder who have never been pregnant.

Certain practical problems may arise in the pregnant epileptic patient. A convulsive seizure occurring in late gestation may be incorrectly diagnosed as eclampsia and unnecessary obstetric procedures instituted. A history of previous convulsive attacks and negative findings of toxemia would suggest the correct diagnosis. Another difficult problem is presented by the patient whose epilepsy is severely aggravated by pregnancy and whose mental deterioration seems to be accelerated by repeated childbearing. Sterilization is indicated if the patient's mental and nervous health is suffering severe impairment. Induced abortion for eugenic reasons is not justified in the state of our present knowledge concerning the hereditary aspects of epilepsy.

ACUTE SITUATIONAL REACTIONS

Certain patients may display sudden excited, often violent, patterns of behavior which defy psychiatric classification in response to the acute

psychologic situation caused by pregnancy. These appear to be due to an increasing accumulation of tension and anxiety in relation to the situation with a sudden discharge of this energy in violent, disturbed behavior, often directed toward the injury of others. One type of reaction is the "Frenzy of Montgomery" of the older obstetricians. This occurs when the head sweeps across the pelvic floor and dilates the vulva, the patient becoming highly excited, cursing profanely at the physician, and being extremely difficult to control, but within a few moments regaining composure and apologizing for her behavior. Another type is the explosive excitement, uncontrolled behavior, prolonged weeping, or impulsive efforts at self-destruction of the unmarried woman who finds herself pregnant. Similar types of uninhibited, excited behavior may be manifested by the married woman who fears another pregnancy. It is quite possible that some of the impulsive infanticides occur in this manner, especially in unmarried mothers who cannot face the stigma associated with return to their own communities. The desertion of children, as shown in Case 7, may occur on the basis of panic and desperation in the face of an acute, intolerable situation. These behavior patterns can often be better comprehended as understandable reactions of a desperate and frightened human being rather than as psychiatric entities. Usually the disturbed behavior is of short duration, often disappearing immediately when a solution for the situation is found.

DIAGNOSIS

It requires no diagnostic acumen to recognize the presence of a puerperal mental disorder but this gross diagnosis has neither therapeutic nor prognostic value. For these purposes it is necessary to make an early and precise psychiatric diagnosis and this is often difficult in an excited and confused patient because of the amorphous character of the reaction. In some cases a history of previous attacks of mental disorder with a description of the psychotic behavior and subsequent course may establish the diagnosis. The time of onset of the psychosis, whether gestational, puerperal, or postpuerperal, is usually of little diagnostic value. It has been shown⁶⁶ that certain mental disorders are most likely to begin in the first week postpartum, while others more usually appear at the end of three weeks, etc. However, it must be realized that these figures are statistical averages and are not a valid basis for diagnosis in an individual case.

The best method of reaching a correct diagnosis is by a minute study of the lifelong personality and a careful evaluation of the clinical psychiatric picture, seeking for major trend patterns. The physician is prone to overvalue the less important symptoms of mental clouding and confusion and to make an erroneous psychiatric diagnosis of a toxic state. The greatest number of mistakes are made in diagnosing a "toxic psychosis" when, in reality, the confused state is merely masking the underlying manic-depressive or schizophrenic disorder. Even the presence of a physical state of toxicity is not conclusive evidence that the accompanying psychosis is a toxic delirium. Inasmuch as the whole plan of treatment, the problem of future pregnancies and the management of the patient after recovery are dependent upon a correct diagnosis, it is essential to have competent psychiatric consultation.

PROGNOSIS

The prognosis for recovery of the whole group of major puerperal psychoses is about 70 to 75 per cent.^{82, 92, 96} This figure means only that

nearly all the manic-depressive and delirious patients and a few of the schizophrenics will recover. It is not correct to state that any puerperal case has a 75 per cent chance of recovery inasmuch as the actual chances are much less if she has a schizophrenic psychosis.

TREATMENT

The early recognition of the presence of a puerperal mental disorder is of greatest importance in the correct management of the case. Too often the attending physician unconsciously refuses to admit the existence of a psychosis or allows the patient to drift into a deplorable condition while he misleads himself with the naïve and wistful hope that "everything will be all right in a day or so." Due to the constant overactivity, excitement and uncooperativeness, these patients rapidly become toxic, exhausted, dehydrated, and malnourished with consequent prolongation of mental convalescence.

The therapeutic efforts of the attending obstetrician should be directed toward the protection of both the mother and child from injury and attempts to improve the maternal physical health as rapidly as possible. Any infection or toxic condition should receive appropriate treatment. The patient should be placed in a secure, screened, single room at once and constant nursing supervision be maintained to prevent suicide or escape. Every effort should be made to avoid physical restraint by supplying adequate nursing service. Exhaustion should be prevented by the judicious use of sedatives, changing the drug frequently to avoid cumulative effects. The state of nutrition should be watched carefully and tube feedings instituted at once if sufficient nourishment is not taken. If dehydration occurs, intravenous infusions should be utilized. Blood transfusions should be used when indicated. Usually it is wise to place the baby on a feeding formula and to suspend maternal mammary function, inasmuch as it will be an exhausting procedure to attempt to empty the breasts, and it is not safe to allow the infant to nurse.

No specific therapy has proved to be of any value. Occasional successes have been reported with hormone therapy, but there is no valid evidence of its efficacy and other physicians have been unable to duplicate the results. Some investigators, believing that an otherwise asymptomatic infective process was causing the psychosis, have used mixed vaccines.^{63, 65} This form of therapy probably has little value.

Psychiatric consultation should be secured at the earliest possible moment. Usually a more rapid convalescence will occur if the patient is transferred to a mental hospital where appropriate psychotherapeutic measures can be instituted.

PROBLEMS OF MANAGEMENT

The question of induced abortion is always raised in those cases in which mental illness and pregnancy occur synchronously. This problem is too frequently approached with little actual data and the decision is made on the basis of the physician's personal predilection and bias. There is really only meager information on which to base conclusions. If pregnancy occurs in a patient already mentally ill, there is no way of predicting the effect of this gestation; some patients may show mental improvement, others become worse. No one can safely predict the effect of abortion in these cases. Some patients may improve when the strain of pregnancy is removed; many remain the same, while others become

worse. In 1933, Robinson⁸² polled 95 British psychiatrists and an overwhelming majority believed that abortion in these cases was not justified. The same general opinion was held for those cases of mental disorder appearing during pregnancy. There appeared no conclusive evidence that the mental illness would be ameliorated by induced abortion and some felt that it might be made worse by the operative shock and emotional upheaval sometimes associated with this procedure.

At the present time, the majority of physicians believe that abortion is justified only when the maternal physical or mental health is in jeopardy. There is little evidence proving that induced abortion has a therapeutic value in arresting the development of a mental disorder in predisposed individuals or those already suffering from mild mental disturbances. Furthermore, the majority of puerperal psychoses spontaneously progress to recovery without permanent psychic damage. The final decision will depend upon the individual case but a positive conclusion should not be reached on the basis of a naïve belief that an abortion will solve the emotional conflicts, terminate a psychosis (except an obvious toxic delirium) or prevent a mild mental disorder from becoming worse or possibly permanent.

The question of termination of pregnancy in these cases is usually connected with the whole problem of induced abortion for eugenic purposes. It is usually argued that the child will probably be a mental misfit since the mother was mentally disordered. There is no valid scientific evidence that this is true. Our knowledge of the hereditary factors in the production of mental disease becomes less conclusive as we learn more about the factors of training, early environmental influences and psychologic conditioning. In view of the chaotic state of our knowledge concerning these hereditary factors, it becomes obvious that no one can predict with any certainty as to the mental caliber of these offspring, and destruction of the unborn on the basis of guesswork and superstition cannot be justified.

Whether these patients who have had puerperal psychoses should undergo further pregnancies often presents a difficult problem. Certainly no pregnancy should occur for at least two or three years after convalescence from the mental disorder. The final decision should be reached only after consideration of all factors. Among these are the patient's wishes and fears, her religious beliefs and possible feelings of guilt as well as all of the physical, physiologic, socioeconomic, and toxic factors which had etiologic significance. The type of psychosis from which she suffered will be of great importance in reaching a decision. Further pregnancies should not be permitted if a schizophrenic psychosis has occurred. Manic-depressive patients may have recurrent attacks of increasing severity, but cases have been reported with a psychotic episode in the first pregnancy and no further difficulty until the sixth gestation. Some psychoneurotic patients find their life load increased intolerably by repeated pregnancies and conception should be prevented before their meager capacity for adjustment is exceeded. On the other hand, if the patient has had a toxic psychosis, she may be able to withstand further gestations without psychic disturbances if the physical status is improved.

The patient's attitude and wishes regarding further pregnancies should receive consideration. A patient who has had a puerperal attack of mental disorder may be terrified at the prospect of another pregnancy. For these individuals, the marital life may become a torment

and the satisfaction and pleasure in sexual relationships ruined by the ever-present fear of pregnancy and its accompanying psychosis. Contraceptive measures may be satisfactory if the patient is intelligent and reliable and if there is no anatomic contraindication. However, the fear of contraceptive failure may be sufficient to ruin the marital happiness and serve as a constant source of apprehension. Sterilization should be undertaken if absolute contraception is necessary.

PRODROMAL MANIFESTATIONS

A study of case histories of puerperal psychoses reveals that usually warning signs appear during the gestational period. However, it is not always easy to evaluate the nervous reactions of a pregnant woman since many bizarre psychologic manifestations may occur without subsequent psychosis. Probably the best single index is the attitude of the patient to her pregnancy and any changes in this attitude which may occur during gestation. An attempt to produce an abortion is indisputable evidence that she does not desire the pregnancy. This rejection may also be expressed by prolonged bouts of weeping, expressions of rancor against the husband, or by irritable references to the unenviable position of women in general and herself in particular. Other indications of an unwholesome mental attitude are irritability, prolonged temper tantrums with little provocation, and evidences of discontent. One of the most common symptoms is increasing tension with excessive anxiety and concern over trivialities, the patient becoming apprehensive and panicky without adequate reason. Flightiness, disconnection in thought and speech, unwarranted suspicions and the occasional production of apparently meaningless, and irrelevant ideas are to be regarded with concern. Probably the most serious manifestation is a progressive, sustained change in personality, especially when it includes suspiciousness and withdrawal. Wide emotional swings from depression to elation may presage a manic-depressive episode. If the above manifestations are obvious and excessive, the physician should consider the possibility of an oncoming mental disorder, especially if the puerperium is associated with toxicity, exhaustion, or psychic shock.

PREVENTION

Modern medical opinion constantly emphasizes the treatment of the patient as a whole person rather than regarding him as a collection of malfunctioning organs operating in a social and emotional vacuum. The modern obstetrician no longer considers gestation to be solely a pelvic phenomenon but is interested in all of the interrelationships of the whole organism under the stimulus of pregnancy. At the present time, obstetrics has achieved a high standard in the physical care of patients, but insufficient attention has been given to the psychic aspects of pregnancy. The obstetrician is just as responsible for the prevention of mental disturbances in his patients as he is for the prevention of eclampsia.

The present discussion has suggested that not all women have reached a psychic and emotional maturity sufficient to withstand the impact of pregnancy and motherhood. While the physician cannot prevent the marriage and impregnation of these individuals, he can serve a useful purpose in two ways: He can promote a better standard of mental hygiene for the young women in his community so that they reach a simultaneous emotional and physical maturity, emancipated from dependence and unwholesome parental attachments, ready for a healthy

sexual marital adjustment and motherhood. Second, he can refrain from suggesting matrimony and motherhood as a cure-all for personality disorders and neurotic disturbances. Marriage and pregnancy impose new burdens upon the individual rather than relieve him of his previous disabilities and maladjustments. It would be more reasonable to advocate treatment of the personality disorder before exposing the already vulnerable individual to the strain of either marriage or pregnancy.

No obstetrician would wish to supervise a pregnancy without evaluating the cardiac and renal reserve and without knowing whether the pelvic outlet was adequate. He should be equally unwilling to bear this responsibility without some evaluation of the patient's psychic reserve. The initial history and all the subsequent discussions should be designed to supply answers to the following questions: What is her constitutional psychologic fitness for pregnancy and motherhood? What personality disabilities does she have which are a source of danger? What are the social, economic, marital, and moral problems and conflicts which confront her? What are her fears and anxieties? What is her real attitude toward this pregnancy and why does she have such reactions? What are the factors in her past life that shaped her personality—is the end result wholesome and capable of bearing stress, and, if not, how can it be understood and improved? Such a history will also reveal previous neurotic and psychotic episodes as well as lifelong instability and inadequacy. If time, tact, and patience are employed, the answers to these questions will be forthcoming, and it will be possible to outline a therapeutic program. There should be ample opportunity for the patient to discuss freely her fears and problems. Often merely bringing out these difficulties openly will give considerable relief, and common sense advice from the physician will solve most of the remainder. However, he should avoid a too critical and authoritative attitude since this often makes patients either resentful and uncooperative or so ashamed of their problems that they avoid discussion. Rather, he should attempt kindly understanding and should help the patient to find better ways of meeting her problems. At times, more direct action will be necessary. For example, if the husband's attitude or behavior is contributing to the unwholesome situation, the physician should not hesitate to discuss the matter frankly with him and attempt to enlist his cooperation. Whatever the problem may be, a wholehearted effort should be made to reach some solution before the time of delivery. Some problems may present an insoluble dilemma, but the patient may still be helped by a frank discussion and a wholesome change in attitude toward the unsatisfactory situation. If this program is followed, the patient will approach term with more confidence and stability and will be better able to withstand any untoward physical complications which may occur.

The obstetrician has shown that he is able to prevent most of the physical disasters of the puerperium. It is also his duty to assume an equal interest in the mental welfare of his patients, for as Gregory⁶⁰ has observed, "A sunny room and plenty of fresh air are not going to prevent the outbreak of a psychosis if the relationship toward the husband and the outlook for mutual respect and healthfulness are dark and humiliating. It is of little avail to give generous advice on the matter of physical hygiene and keep absolutely quiet about rotten social conditions . . . our constant effort must be toward the goal of better mental hygiene."

REFERENCES

1. Hippocrates: Epidemics I, III, New York, Wm. Wood & Co.
2. Esquirol: *Maladies Mentales*, Paris, 1838.
3. Conolly, J.: *Lancet* 1: 349, 1846.
4. Macdonald, J.: *Am. J. Insan.* 4: 113, 1847.
5. Editorial: *Lancet* 1: 318, 1848.
6. Webster: *Lancet* 2: 611, 1848.
7. Marcé, L. V.: *Traite de la Folie des Femmes Enceintes des Nouvelles Accouchees et des Nourrices*, Paris, 1858.
8. Hughson, J. S.: *Med. & Surg. Reporter* 32: 104, 1875.
9. Hengst, D. A.: *Med. & Surg. Reporter* 39: 134, 1878.
10. Barker, F.: *The Puerperal Diseases*, New York, 1878, D. Appleton-Century Co., 10: p. 161.
11. Kent, J. T.: *Am. Med. J.* 7: 180, 1879.
12. Beates, H.: *Med. & Surg. Reporter* 42: 425, 1880.
13. Carr, J. M.: *Cincin. Lancet Clinic* 7: 537, 1881.
14. Fraser, D.: *Glasgow M. J.* 24: 369, 1885.
15. Macleod, M. D.: *Brit. M. J.* 2: 239, 1886.
16. Wigglesworth, J.: *Liverpool M.-Chir. J.* 6: 349, 1886.
17. Brooke, H.: *J. Nerv. & Ment. Dis.* 14: 361, 1887.
18. Clark, A. C.: *J. Ment. Sc.* 33: 169, 372, and 487, 1887-8.
19. Bowers, J. E.: *Northwest. Lancet* 8: 32 and 43, 1888.
20. Hyzer, E.: *Med.-Leg. J.* 7: 1, 1889.
21. Hirst, B. C.: *J. A. M. A.* 12: 29, 1889.
22. Sprigg, W. M.: *Am. J. Obst.* 30: 537, 1894.
23. Harrison, G. B.: *Am. J. Obst.* 30: 529, 1894.
24. Tomlinson, H. A.: *Am. J. Insan.* 56: 69, 1899.
25. Hirsch, W.: *Med. Rec.* 57: 10, 1900.
26. Lane, E. B.: *Boston M. & S. J.* 144: 606, 1901.
27. Hattie, W. H.: *Montreal M. J.* 31: 710, 1902.
28. Jones, R.: *Am. J. Insan.* 59: 601, 1903.
29. White, E. W.: *Brit. M. J.* 1: 306, 1903.
30. Jones, R.: *Brit. M. J.* 1: 199, 1903.
31. Hummel, E. M.: *New Orleans M. & S. J.* 57: 373, 1904.
32. Raw, N.: *Edinburgh M. J.* 20: 118, 1906.
33. Cowles: *J. Nerv. & Ment. Dis.* 33: 788, 1906.
34. Rigden, A.: *Brit. M. J.* 2: 1253, 1906.
35. Ostrander, H.: *J. Mich. M. Soc.* 6: 49, 1907.
36. Brown, H. E.: *Transvaal M. J.* 3: 310, 1908.
37. Recksher, C.: *Boston M. & S. J.* 161: 142, 1909.
38. Ballintine, E. P.: *New York State Med. J.* 9: 460, 1909.
39. Clark, G.: *J. Ment. Sc.* 59: 67, 1913.
40. Sandy, W. C.: *J. Med. Soc. New Jersey* 10: 230, 1913.
41. Huggins, R.: *Am. J. Obst.* 69: 244, 1914.
42. Langdon, F. W.: *The Lancet-Clinic*, March 13, 1915.
43. McCarthy, D. J.: *Am. J. Obst.* 72: 269, 1915.
44. Bishop, E.: *Long Island M. J.* 10: 49, 1916.
45. Barnes, F. M.: *Surg., Gynec. & Obst.* 22: 579, 1916.
46. Brown, S.: *J. Nerv. & Ment. Dis.* 43: 518, 1916.
47. Gardner, W. E.: *Kentucky M. J.* 15: 206, 1917.
48. Harrar, J. A.: *New York Lying-In Hospital Bulletin* 11: 123, 1917.
49. Allen, C. L.: *Med. & Surg.* 2: 350, 1918.
50. Norbury, F. P., and Dollear, A. H.: *J. A. M. A.* 74: 249, 1918.
51. DeForest, H. P.: *Am. J. Obst.* 77: 277, 1918.
52. Schenck, S. B.: *Am. J. Obst.* 78: 596, 1918.
53. Cornell, E. L.: *Surg. Clin. Chicago* 3: 1297, 1919.
54. Zapiola, J. G.: *Abst. J. A. M. A.* 77: 823, 1921.
55. Bear, J.: *Virginia M. Monthly* 48: 151, 1921.
56. Riggs, C. E.: *Minnesota Med.* 5: 375, 1922.
57. Peachall, G. E.: *J. Ment. Sc.* 69: 83, 1923.
58. Wright, H. W.: *Calif. State J. M.* 21: 170, 1923.
59. Armstrong-Jones, R.: *Lancet* 1: 1297, 1923.
60. Gregory, M. S.: *AM. J. OBST. & GYNEC.* 8: 420, 1924.
61. *Proc. Royal Soc. Med.* 17: 1, 1924.
62. Bourne, A. W.: *J. Obst. & Gynaec. Brit. Emp.* 31: 251, 1924.
63. Lalor, P.: *Med. J. Australia* 2: 529, 1924.

64. Wilson, E. A., and Christie, T.: *Brit. M. J.* 2: 797, 1925.
65. Lalor, P.: *Med. J. Australia* 1: 247, 1926.
66. Streckler, E., and Ebaugh, F.: *Arch. Neurol. & Psych.* 15: 239, 1926.
67. Lord, J. R.: *J. Ment. Sc.* 73: 390, 1927.
68. Hopwood, J. S.: *J. Ment. Sc.* 73: 95, 1927.
69. Mellroy, A. L.: *Lancet* 1: 379, 1928.
70. Stone, C. W., and Karnosh, L. J.: *Ohio State M. J.* 24: 29, 1928.
71. Zilboorg, G.: *Am. J. Obst. & Gynec.* 15: 145, 1928.
72. Zilboorg, G.: *J. Nerv. & Ment. Dis.* 68: 370, 1928.
73. Zilboorg, G.: *Am. J. Psych.* 8: 733, 1929.
74. Saunders, E. B.: *Am. J. Psych.* 8: 669, 1929.
75. Alpers, B. J., and Palmer, H.: *J. Nerv. & Ment. Dis.* 70: 465, 606, 1929.
76. Menninger, W.: *J. Kansas M. Soc.* 31: 391, 1930.
77. Zilboorg, G.: *Am. J. Psych.* 10: 927, 1931.
78. Mengert, W.: *Ment. Hygiene* 15: 299, 1931.
79. Solomons, B.: *J. Ment. Sc.* 77: 701, 1931.
80. Cantor, S. J.: *Med. J. Australia* 2: 208, 1932.
81. Crowder, R.: *J. Iowa State M. Soc.* 22: 583, 1932.
82. Robinson, A. L.: *J. Obst. & Gynaec. Brit. Emp.* 40: 39, 1933.
83. Hall, D., and Mohr, G.: *Ment. Hygiene* 17: 226, 1933.
84. Parfitt, D. N.: *J. Ment. Sc.* 79: 501, 1933.
85. Anderson, E. W.: *J. Ment. Sc.* 79: 137, 1933.
86. McGoogan, L.: *AM. J. OBST. & GYNEC.* 25: 792, 1933.
87. Parfitt, D. N.: *J. Ment. Sc.* 80: 43, 1934.
88. Bamford, C. B.: *J. Ment. Sc.* 80: 58, 1934.
89. Morton, J. H.: *J. Ment. Sc.* 80: 64, 1934.
90. Smith, B.: *J. Kansas M. Soc.* 35: 203, 1934.
91. Frumkes, G.: *J. Nerv. & Ment. Dis.* 79: 540, 1934.
92. James, G. W. B.: *Lancet* 1: 1515, 1935.
93. Wilson, R.: *J. Kansas M. Soc.* 36: 104, 1935.
94. Glueck, B.: *Med. Clin. North America* 19: 927, 1935.
95. Davidson, G. M.: *Am. J. Psych.* 92: 1331, 1936.
96. Harris, J. S.: *Brit. M. J.* 1: 835, 1936.
97. Long, R. H.: *South. M. & S.* 98: 311, 1936.
98. Karnosh, L. J., and Hope, J. M.: *Am. J. Psych.* 94: 537, 1937.
99. Atkin, I.: *Lancet* 1: 434, 1938.
100. Hirst, J., and Strousse, F.: *Am. J. M. Sc.* 196: 95, 1938.
101. Fagan, R.: *West. J. Surg.* 46: 639, 1938.
102. McGeorge, J.: *Med. J. Australia* 2: 671, 1938.
103. Williams, H. B.: *Med. J. Australia* 2: 677, 1938.
104. Piker, P.: *AM. J. OBST. & GYNEC.* 35: 901, 1938.
105. Baptisti, A.: *AM. J. OBST. & GYNEC.* 35: 818, 1938.
106. Benedek, T., and Rubenstein, B.: *Psychosom. Med.* 1: 245 and 461, 1939.
107. Smalldon, J. L.: *Am. J. Psych.* 97: 80, 1940.
108. Reider, N.: *Arch. Neurol. & Psych.* 44: 1069, 1940.
109. Cruickshank, W. H.: *Canad. M. A. J.* 43: 571, 1940.
110. Kilpatrick, E., and Tiebout, H.: *Am. J. Psych.* 6: 145, 1926.

Editorial

The Perpetuation of Error

THIS rather provocative title should call particular attention to the Chairman's Address at the last meeting of the section on obstetrics and gynecology of the American Medical Association.* The choice of subject is relevant and significant. Although the address may arouse favorable comment and likewise criticism, this should prove most desirable, and there is little doubt that the majority of thinking men will be in accord with the principles enunciated by Dr. Miller.

Errors are common enough in every field of endeavor. It is their perpetuation which constitutes a source of danger. Dr. Miller calls attention to numerous repetitious errors committed daily in the practice of our specialty, many of which are engendered by custom but for others he places the responsibility upon the sacrifice of quality in many contributions to medical literature. He feels very strongly that much of this can be traced to the insistent demands of department heads upon their often less mature staff members for "original research" articles. Many of these he claims are mediocre, digressive, and unsound; the conclusions which they present are insufficiently documented and inadequately checked. These contributions in Dr. Miller's belief perpetuate errors and false notions. Clothed as novelties, they, in addition, are readily seized upon by multitudinous lay writers who are flooding the popular magazines with their effusions. The latter may even mold public opinion beyond any control by the medical profession.

The fallacious assumption that the results observed in animal research can be transmitted directly to human experiences in gynecic practice, is another persistent error pointed out by Dr. Miller. For example, confusion has been added to confusion by the multitude of hormone preparations exuberantly reported upon by a multitude of observers. The impression is gained that, very frequently, these are subsidized by interested manufacturers, although it may be said in favor of the latter that their own well-conducted laboratories have added greatly to our knowledge in this field.

An advance must be acknowledged in this trend to corrective measures in diseases and disturbances of the female generative organs aside from those of a purely mechanical character which dominated and still dominate so much of gynecologic practice. The preservation of essential organs, in whole or in part, by the avoidance of radical pelvic surgery, unless definite pathologic evidence dictates the latter course,

*Journal of the American Medical Association, September 13, 1941.

requires that more intimate knowledge of physiologic relationships which has so often been ignored in the past because of erroneous principles based upon insufficient knowledge.

Dr. Miller's critical attitude toward delivery service as conducted in many homes or in poorly equipped hospitals is well taken. However there is no immediate solution and it must be admitted that the experiences of many general practitioners in obstetrics are better than those of many hospital services.

The general practitioners, especially in isolated communities, often far removed from modern hospital facilities, do not write in as boasting terms as do the urban specialists. Their results are good provided the initial make-up of the home-delivering doctor includes, as it does usually, integrity of character, certain technical ability, requisite patience and sound judgment.

We need not teach dual standards for home and hospital care. But the home delivery cannot at present be disregarded; it is inefficiency which needs be set aside in both instances. The hospital must still contend with tendencies toward interference, over-zealousness and radical management of labor.

Dr. Miller has spoken well and wisely. It remains for other teachers in this field to indicate the path of improvement and to eliminate what he so courageously describes as the perpetuation of errors in our particular field of medicine. Unfortunately this is duplicated elsewhere in perhaps equal volume.

Society Transactions

AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS, AND ABDOMINAL SURGEONS

*FIFTY-FOURTH ANNUAL MEETING, THE HOMESTEAD,
HOT SPRINGS, VA., SEPTEMBER 11, 12, 13, 1941*

The following papers were presented:

- President's Address. (Observation in the Art of Medical Illustration.)** Dr. Frederick H. Falls, Chicago, Ill.
- Gonadotropic Hormone Concentration in Emesis Gravidarum.** Dr. F. J. Schoeneck, Syracuse, N. Y. (For original article, see page 308.)
- Transverse Plication of the Rectum for the Reduction of Large Rectoceles.** Dr. Walter T. Dannreuther, New York, N. Y. (For original article, see page 286.)
- Management and Outcome of Labor in 742 Women With Borderline Pelves.** Dr. J. Bay Jacobs, Washington, D. C. (For original article, see page 267.)
- Malignancy of the Ovaries.** Dr. James R. Goodall, Montreal, Canada. (For original article, see page 210.)
- The Treatment of Gonorrhea in the Female with Sulfathiazole.** Drs. Dudley R. Smith, and Rogers Deakin, St. Louis, Mo. (For original article, see page 296.)
- Study and Management of the Cervix Before Hysterectomy.** Dr. Henry L. Darner (by invitation), Washington, D. C.
- Granulosa and Theca Cell Tumors of the Ovary.** Dr. D. Nelson Henderson (by invitation), Toronto, Canada. (For original article, see page 194.)
- Endometriosis.** Dr. Walter R. Holmes (by invitation), Atlanta, Ga. (For original article, see page 255.)
- A Study of 104 Cases of Uterine Fibroids Associated With Arterial Hypertension.** Dr. W. O. Johnson (by invitation), Louisville, Ky. (For original article, see page 231.)
- Pathology of the Embryo and Abortion.** Dr. A. K. Paine, Boston, Mass. (For original article, see page 245.)
- An Improved Method of Uterine Closure in High Classical Cesarean Section.** Drs. Milton G. Potter, and Norman W. Elton, Buffalo, N. Y. (For original article, see page 303.)
- Hysterectomy in Pregnancy, Labor and the Puerperium.** Dr. Gerald W. Gustafson, Indianapolis, Ind. (For original article, see page 221.)
- Occiput Posterior—A Normal Presentation.** Dr. L. A. Calkins, Kansas City, Mo. (For original article, see page 277.)
- A Comparison of Thyroid Extract and Iodine Therapy in the Prevention of Toxemia of Pregnancy.** Drs. Emmett D. Colvin, R. A. Bartholomew, and W. H. Grimes, Atlanta, Ga. (For original article, see page 183.)
- Midline Episiotomy.** Drs. J. P. Pratt, C. P. Hodgkinson, and C. R. Kennedy, Detroit, Michigan. (For original article, see page 292.)

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Physiology of Pregnancy

Bowman, Donald E.: The Use of a Reducing Factor of Pregnancy Urine in the Diagnosis of Pregnancy, *J. Lab. & Clin. Med.* 24: 1072, 1939.

To obviate time and expense, a chemical test for pregnancy would be of distinct value. Urinary pregnancy hormones are known to contain a reducing factor, and this substance might be developed for use in such a chemical test.

The technique of the test is as follows: 12 c.c. of a fresh specimen of urine, specific gravity 1.020, are brought to a pH of 7.4 with 10 per cent sodium hydroxide; 9 c.c. of acetone are added and the precipitate centrifuged. The supernatant liquid is adjusted to a pH of 5.9 with 66 per cent sulfosalicylic acid. If a precipitate is formed, it is discarded; 1 c.c. of Sörensen's phosphate buffer is added to the liquid plus 18 c.c. of acetone and stirred and centrifuged for ten minutes. The supernatant fluid is withdrawn and the viscous precipitated layer contains the pregnancy reducing and gonadotropic factors. These are dissolved in 5 c.c. of water and 1 c.c. is treated with a few drops of 5 per cent starch solution and heated in the water bath at 38° C. until starch iodine color remains. In a total of 303 cases there were 108 correct positives and 80 correct negatives. The percentage of accuracy is 98.4 per cent. It is believed that the use of this reducing factor is a valid basis for a chemical test for pregnancy.

W. B. SERBIN.

Kraus, Anny, and Koenigstein, Rudolf: Experiences With the Pregnancy Test of Kapeller-Adler Histidinuria in Pregnant Women, *Chinese M. J.* 59: 129, 1941.

The positive histidine test during pregnancy, though not specific, must be considered a very important sign for the diagnosis of pregnancy. Morning specimens of urine give the best results.

C. O. MALAND.

Effkemann, G., and Werle, E.: Significance of Diminished Histaminase Activity of the Blood in Pregnancy in Initiating Abortion, *Zentralbl. f. Gynäk.* 64: 221, 1940.

The authors report an increase in the histamine-storing ability of the blood to 10 times normal by the sixth to eighth month of pregnancy as a result of increase in histaminase. A large amount of histaminase is found in the maternal blood and circulating through the placental tissues. The significance of the release of extra histamine into the circulation lies in its effect on tissue permeability. Outside of the inactivating effect of histaminase in pregnancy other substances prevent the full contraction-stimulating effect of histamine on the uterus.

In cases of abortion, the authors found the maternal blood and serum were able to take up much more histamine than in normal pregnancy, regardless of the type of abortion, indicating a much lower blood-histamine content in this condition. In cases of habitual abortion, the authors believe, there is a constitutional adrenal

cortex defect involving the failure to influence adequate histaminase storage, as well as corpus luteum and vitamin E insufficiencies. Blood histaminase values return to normal in a few days after the death of the ovum in early pregnancy as effect of the disappearance of placental histaminase. It should be remembered, however, that histaminase activity is also decreased in normal pregnancy with coincident infection, which may perhaps explain the occurrence of abortion or premature labor in these cases. The author suggests the administration of histaminase in threatened or habitual abortion.

R. J. WEISSMAN.

Cope, C. L.: The Diagnostic Value of Pregnanediol Excretion in Pregnancy Disorders, Brit. M. J. 2: 545, 1940.

Pregnanediol, produced by corpus luteal and placental activity, is present in the urine only in the luteal phase of normal menstruation and during pregnancy. On this premise the author studied over 100 cases of pregnancy, some 75 of which were seriously abnormal, in an effort to evaluate pregnanediol analysis as a diagnostic aid in obstetric disorders.

After discussing the normal behavior of pregnanediol and the means of estimating its secretion, the author summarizes his findings as to the value of pregnanediol in obstetric diagnosis.

Pregnancy is the only known condition in which amenorrhea is associated with the continued excretion of pregnanediol; hence this test is of importance in the diagnosis of early pregnancy. Consequently, the absence of pregnanediol in the urine in the case of amenorrhea usually means the absence of pregnancy. In both cases 2 or more tests must be made to be of significance. In a woman with signs and symptoms of a threatened abortion if pregnanediol is persistently absent in 2 or more determinations, 1 of 3 conditions is suggested, an inevitable, incomplete, or a missed abortion. The clinical findings must be considered to distinguish between these 3 possibilities. The presence of such serious abnormalities can often be detected by tests for pregnanediol when classical signs and symptoms are absent or have not yet appeared. In cases of suspected intrauterine death, pregnanediol determinations may give a clue to the diagnosis or strengthen or confirm a suspicion of the diagnosis.

The author warns that certain factors may affect pregnanediol excretion and lead to a misdiagnosis. These include such conditions as chronic nephritis and toxemias of pregnancy.

In considering the relative merits of the Aschheim-Zondek and pregnanediol excretion tests in the diagnosis of pregnancy disorders, there are advantages, technical, to each. However, as to the comparative value of each test no study has as yet been made.

FRED L. ADAIR AND H. W. PHILLIPS.

Kelso, Rich E.: A Twenty-Four-Hour Test (Aschheim-Zondek Modification) for the Diagnosis of Pregnancy, Am. J. Clin. Path. 10: 293, 1940.

Kelso points out that the employment of rabbits in the Friedman test has certain disadvantages: they are more expensive than mice, more difficult to breed, they have to be isolated for thirty days prior to use, and a small percentage of them do not respond to pregnancy urine hormone. In order to achieve greater economy and convenience and a more rapid diagnosis, the author developed a modified test in which rats are employed and which requires only twenty-four hours for its completion.

The test consists of using four immature female rats between twenty-two and forty days old. Two of the rats are injected with 1 c.c. of the urine at 9 A.M., 1 P.M., and 5 P.M. on one day, and are killed and examined at 9 A.M. the next morning. The two other rats are injected with 0.5 c.c. of the urine at the same intervals on two successive days, and the animals are killed and examined on the

fourth day, that is, seventy-two hours after the first injection. These latter tests are performed primarily for control purposes.

A total of 130 urine specimens including cases of normal pregnancies, ectopic pregnancies, missed and threatened abortions, endocrine dyscrasias, etc., were tested. In five instances the twenty-four-hour test showed a positive reaction, while the seventy-two-hour test was negative. Clinically these patients were eventually shown not to be pregnant. In 125 cases there was perfect correlation between the twenty-four- and the seventy-two-hour tests. The author concludes therefore, that this new twenty-four-hour test on rats is superior to any previously described and fulfills the requisites of a reliable and rapid pregnancy test.

J. P. GREENHILL.

Daniel, S. P., and Tien, B. S.: The Significance of Pregnanediol in Pregnancy Urine, Chinese M. J. 59: 416, 1941.

The excretion of sodium pregnanediol glucuronide in the pregnancy urine of Chinese women at various stages of gestation agrees with that in Western countries. In a case of twin pregnancy, definitely higher values of pregnanediol were encountered throughout the whole course of gestation. The yield of pregnanediol with isobutyl alcohol as the extracting solvent was found to be only 64 per cent of that with normal butyl alcohol. From the data they have accumulated so far they consider that it is still premature to regard the excretion of sodium pregnanediol glucuronide in the urine of pregnant women as an accurate index in the metabolic process of the corpus luteum hormone.

C. O. MALAND.

Paddock, Richard: A Test for Pregnancy, South. M. J. 34: 174, 1941.

The author has originated a biologic test for pregnancy which is based upon certain changes in the external genitalia of the guinea pig. The vagina of this test animal is occluded by a membrane which is absent for about forty-eight hours during the estrous period, which has a fifteen- to seventeen-day cycle. Injection of estrogenic substances, or the serum of pregnant women causes a disappearance of the vaginal closure membrane. Three thirty- to forty-five-day-old female guinea pigs with closed vaginal membranes are used, and 1.2 to 1.5 c.c. of blood serum is injected subcutaneously into the pectoral region of each animal. The test is read at the end of forty-eight hours and the interpretations are as follows: (a) Positive for pregnancy, if the vagina in each animal is partly open or wide open; if two show patency while the third is closed; (b) negative for pregnancy, if all three, or two of the animals have closed vaginas. Evidence of marked congestion of the genitals or only suggestive signs may be seen. If vaginal patency occurs in two of the three animals between forty-eight and seventy-two hours the test should be repeated. After a one- to two-day interval, the guinea pigs may be used again.

A total of 254 pregnancy tests were performed by the author employing 28 animals; thus an average of 9 tests per animal was obtained. The largest number of times that any pig was used was ninety-five.

The results of this test compared favorably with those obtained with a modified Friedman test routinely employed in the same clinic. The few erroneous results were toward the negative, and there were no known false positive reactions.

Simplicity and economy are the advantages claimed by the author for this biologic test. It is not difficult to learn the changes that occur in the genitalia, and, only a small number of test animals need be maintained.

ARNOLD GOLDBERGER.

Henriksen, Erle: Pregnancy Tests of the Past and the Present, West. J. Surg. 49: 567, 1941.

The author presents a rather complete, precise and at the same time highly amusing summary of practically all known pregnancy tests in a short paper, the

larger part of it taken up by excellent, cartoonlike, descriptive illustrations, beautifully drawn by Ted Bloodhart of the Department of Medical Art.

Henriksen's concluding statements read as follows: In reviewing the methods offered from time to time we have been impressed by the ingenuity of the empirical tests devised for the diagnosis of pregnancy. The Egyptians, 3,300 years ago, recorded pertinent observations upon the urine of gravid females indicating the presence of a substance capable of inducing the germination of seeds, an action similar to that characteristic of current biologic tests. As it is with many of the other so-called modern suggestions, we must admit the truth of the proposition formulated by Aristotle, "probably all art and all wisdom often have already been fully explored and again quite forgotten." Notwithstanding the progress of medical knowledge, an infallible diagnosis is still awaited more hopefully today than ever before. Thus, as it has been down through the ages, the question remains, "Is she pregnant? (see Fig. 10)."

HUGO EHRENFEST.

Weisman, Abner L., and Coates, Christopher W.: The Frog Test (*Xenopus laevis*) as a Rapid Diagnostic Test for Early Pregnancy, *Endocrinology* 20: 141, 1941.

Xenopus laevis is the South African clawed toad.

The authors list the investigators in this field, all of whom established the diagnosis of pregnancy after injecting the *Xenopus laevis* with concentrates of APL derived from urine. The technique consisted of injecting 1 c.c. of a simple alcohol or acetone extract of the suspected urine into the dorsal lymph space of from 5 to 12 animals. The extrusion of hundreds of macroscopic eggs six to eighteen hours after injection was considered a positive reaction. Apparently, the results of 600 collected tests were in agreement with Aschheim-Zondek test 99 per cent of the time.

The authors then report the results of their own investigative work on 12 imported *Xenopus laevis*. The 12 animals were divided, 2 each in 6 tanks designated as A, B, C, D, E, and F. The animals in A received 1 c.c. of sterile water. The animals in the other tanks were given standardized commercial APL (Parke-Davis antuitrin-S) in varying doses as follows: Tank B, 10 R.U.; Tank C, 50 R.U.; Tank D, 100 R.U.; Tank E, 250 R.U.; Tank F, 500 R.U. All medications were given by subcutaneous injection into the dorsal lymph space. The animals were observed eighteen hours after injection.

Animals in Tanks A, B, and C showed no reaction, in Tanks D and E, marked positive reactions and in Tank F, both animals died. The results of similar experiments repeated in the New York Aquarium are mentioned and corroborate the above findings.

The authors conclude that it is unlikely that the large amount of anterior pituitary-like hormone necessary to produce ovulation in the *Xenopus laevis* could be found in the normal pregnancy urine.

CLAUDE J. EHRENBURG.

Gelle, P., and Driessens, J.: Biochemical Changes of the Blood During the Course of Pregnancy, *Presse méd.* 48: 861, 1940.

The writers performed biochemic studies upon 45 pregnant women. Twenty-five of them were at term while the remaining two groups, in first and second trimesters, each included 10 pregnant women.

The biochemic observations obtained from each of these cases included the plasma and blood chlorides, blood sugars, blood ureas, blood proteins, blood polypeptides, the total nonprotein nitrogen of the blood, evaluation of the serum and globulin fractions of the blood proteins, electrometric determination of the blood pH and the determination of the alkaline reserve.

The authors found no gross disturbances of the biochemic equilibrium of the blood during the course of the pregnancy. Mild variations did occur. These changes

were found essentially in the plasma and blood chlorides, the pH of the blood and in the alkaline reserve. Mild deviations of the nonprotein blood constituents were also noted. From the physicochemical viewpoint gestation is accompanied by a well-compensated but moderate acidosis.

The investigators conclude that the biochemic approach offers insufficiently significant blood chemistry changes to warrant further exploitation of biochemic blood studies to explain the pathogenesis of toxemias of pregnancy.

CLAIR E. FOLSOME.

Cadden, J. F.: The Glutathione Content of Blood During the Puerperium, J. Lab. & Clin. Med. 23: 1266, 1938.

Glutathione is distributed throughout the body in blood and muscle. A study was made of the blood glutathione in a series of 40 cases during labor and the puerperium. The blood was drawn early in labor and immediately following delivery. In addition, determinations in 20 patients were made on the first, third, fifth, seventh, and ninth days of the puerperium; in the remaining 20, on the second, fourth, sixth, eighth, and tenth days of the puerperium. It was found that during labor, blood glutathione increased from an average of 35.9 mg. per 100 c.c. in early labor to 39 mg. immediately following delivery. Following delivery, there is a decrease during the first three days of the puerperium, probably due to blood loss during delivery. From the third to the eighth post-partum days, there is a rapid rise in glutathione, due probably to the formation of new red blood cells which have a higher glutathione content. Between the eighth and tenth days of the puerperium, the concentration of glutathione in the blood maintains a level approximately 18 per cent higher than that noted during labor.

W. B. SERBIN.

Horwitz, O., and Farley, D. L.: Vitamin B Deficiency in Pregnancy as Indicated by a Test for OBT Principle, Surg. Gynec. & Obst. 71: 313, 1940.

Numerous articles have appeared indicating that a deficiency of vitamin B₁ occurs frequently in pregnancy and that this deficiency may be overcome by administration of the vitamin. The symptoms of this deficiency have been reported as polyneuritis, hyperemesis gravidarum, numbness and tingling of the fingers and toes, tenderness of the extremities to pressure, muscular weakness, loss of deep reflexes, anorexia, periodic nausea, glossitis, tachycardia, edema, easily induced fatigue, etc.

Thirteen pregnant women, from a total of 100, studied by a test on blood serum, were found to be low in vitamin B₁ titer.

The OBT level, details of the test described in a previous article, can be raised by the administration of yeast over a four-day period.

Patients judged to be low in vitamin B₁ by this test have a definite tendency to develop neuritic symptoms.

One patient who developed eclampsia, had an adequate titer of OBT.

From this study it would appear that a deficiency of vitamin B₁ in pregnancy has a definite effect upon the appetite.

WILLIAM C. HENSKE.

Ribeiro, Daniel: Vitamin C in Pregnancy, Rev. de gynec. e. d'obst. (Rio de Janeiro) 2: 107, 1940.

This paper summarizes the principal studies and the role which vitamin C plays during pregnancy. The author reports thirty cases of pregnant women on whom he made tests for vitamin C saturation and shows, in conclusion, that all the observations made in the thirty cases showed deficiency in vitamin C.

MARIO A. CASTALLO.

Brieger, Hubertus: Vitamin C Metabolism in Pregnancy, *Ztschr. f. Geburtsh. u. Gynäk.* 121: 80, 1940.

This report is from the department of Physiology at Rostock, headed by Wachholder who has done considerable work with vitamin C. The study was carried out to attempt to determine what happens to vitamin C metabolism in pregnancy under varying conditions of intake. The guinea pig, rat, and rabbit were used. Reports are given on only small numbers of animals and techniques are not described. The results, however, are of considerable interest.

Wachholder and his associates have shown that in both young and old animals, a diet low in vitamin C gives rise to an inability to stabilize oxygen consumption although in older rats this may ultimately be stabilized at a level above the normal. In young growing animals developmental disturbances occur. In general, similar changes occur in the rat, the guinea pig, and the rabbit.

Moriquand reported that the guinea pig on a scorbutic diet remained free of evidence of vitamin C deficiency during the second half of pregnancy but showed such evidence after delivery. The statement is made that the rabbit shows similar findings. Neuweiler, on the other hand, was unable to confirm this and stated that signs of scurvy appeared in the pregnant guinea pig just as quickly as in the nonpregnant. It is this disagreement which Brieger is attempting to settle.

Brieger's observations are based on animals obtaining a diet deficient in vitamin C but containing some.

A superimposed graph of the oxygen consumption per gram minute over a period of nine days in three guinea pigs is shown. The pregnant deficient animal showed the most regular oxygen consumption at about normal level. The pregnant animal on full diet showed considerable variation about this level while gross variations appeared in the nonpregnant deficient animal as evidence of an inability to stabilize oxygen consumption.

Experiments were carried out to determine in vitro the ability of various tissues to produce vitamin C under different conditions. In the guinea pig which was pregnant and had been on a green diet, no significant tissue synthesis could be demonstrated. Tissues of both pregnant and nonpregnant guinea pigs who had been on deficient but not vitamin C free diets showed significant increases in vitamin C content after six hours in normal saline at 37° C. The tissues from the pregnant animals showed a constantly greater increase than those of the nonpregnant. The greatest increase was found in the last part of pregnancy and here all maternal organs apparently synthesized vitamin C. The maternal portion of the guinea pig placenta showed an increase in vitamin C after six hours. The fetus can synthesize little vitamin C.

It is concluded that a protective mechanism is produced in pregnancy in these animals on varying degrees of vitamin C dietary deficiencies. It is to be presumed that the human being acts somewhat similarly. Decrease in tissue vitamin C levels should not at once be considered to be evidence of an avitaminosis in view of the stability of the oxygen consumption in the pregnant deficient animal. Saturation deficits in pregnancy should not be translated at once into terms of deficient intake although this does not mean that an increased intake during pregnancy is not desirable. On the contrary, lower levels of vitamin C in the fetus are demonstrated for the guinea pig when the intake is deficient. The synthesis of vitamin C can protect the mother but not the fetus from scurvy. As well, the deficient mother can develop scurvy quickly under these conditions after delivery.

The questions posed by a study of vitamin C in many obstetric and gynecologic problems are of such interest and probable importance that such information as is available should serve to stimulate work on the subject even though, as in this report, the results do not yet approach finality.

J. L. MCKELVEY.

Gaetgens, G.: Nutrition During Pregnancy in the Light of Present Day Food Rationing, *Med. Klin.* 36: 561, 1940.

An investigation of the food requirements of pregnant women leads Gaetgens to maintain that during gestation a woman weighing 60 kg. (132 pounds) requires

between 2,500 and 3,000 calories daily. She should have between 90 and 100 Gm. of protein, 60 Gm. of fat and between 400 and 500 Gm. of carbohydrate. The intake of table salt should not exceed 5 Gm. a day. The vitamin content should consist of 80 to 100 mg. of vitamin C, 10,000 international units of vitamin A, and 1,500 units of vitamin B.

J. P. GREENHILL.

Stieve, H.: Exit of Intervillous Blood from the Human Placenta, Zentralbl. f. Gynäk. 64: 1570, 1940.

In a well-documented and illustrated report, the author demonstrates the communication between maternal veins and placental intervillous spaces in all parts of the uterine surface of the placenta, in contrast to the idea of a limited, special marginal zone, postulated by some writers, where blood was able to enter the maternal venous system. The appearance of valvelike structures and sphincters in these veins indicates the functioning of some sort of a regulatory mechanism.

R. J. WEISSMAN.

Kropp, Benjamin: The Content and Distribution of Minerals in Human Amnion and Chorion at Term, Anat. Rec. 77: 407, 1940.

The method used by the author was that of microincineration. Both the placental and nonplacental portions of the amnion and chorion were studied. It was found that the cytoplasm of the nonplacental part of the amnion is rich and the nuclei are poor in minerals. The quantity of water soluble minerals, including calcium is low in the cytoplasm. In the placental portion of the amnion, most of the minerals are present just within the cell membrane, except at the base of the cell which is invariably ash free. The basement membrane of the amnion is a mineral-free structure. A small amount of mineral, probably silica, is present in the epithelium of both amnion and chorion. The decidua and connective cells are rich in water-soluble minerals and contain more iron than either the amniotic or chorionic epithelium.

WILLIAM BERMAN.

Becker, R. F., Barth, E. E., and Schulz, M. D.: Fetal Swallowing, Gastro-Intestinal Activity and Defecation in Amnio, Surg. Gynec. & Obst. 70: 603, 1940.

That amniotic fluid may be swallowed by the fetus and that it may serve some nutritive function in the growth process during intrauterine existence is not a new idea.

Under normal physiologic conditions in utero, the guinea pig fetus begins to swallow amniotic fluid about the forty-second day of gestation. This fact is indicated by the presence of a stomach shadow in roentgenograms after the amniotic sac has been injected with 0.4 to 1.0 c.c. of colloidal thorium hydroxide or dioxide (thorad or thorotrast).

The rapidity with which the thorium reaches the fetal stomach after injection and the efficiency with which the material is propagated along the gastrointestinal tract increases with age.

Late in fetal life, usually not before the sixtieth day, defecation begins to occur in amnio as a normal phenomenon. Meconioophagy is also a normal physiologic function of guinea pigs in utero. The cycle of swallowing, defecation, and reswallowing of the thorium-impregnated meconium may be repeated several times before birth.

It has been suggested, but proof is lacking, that the swallowing of the amniotic fluid is important from the standpoint of prenatal water metabolism. It may be significant that swallowing begins when the fetus is just starting to grow at its most rapid rate. Comparison with conditions in the rabbit suggests the probability that at this point the efficiency of the fluid exchange from the placenta via the blood stream is declining and that the fetus makes use of its reserve of fluid in the amniotic sac.

WILLIAM C. HENSKE.

Dietrich, Doris: *The Variation of Duration of Pregnancy in Brood Animals and Its Cause*, Ztschr. f. Geburtsh. u. Gynäk. 121: 296, 1940.

This reports a study of the literature dealing with the duration of pregnancy in various large domestic animals. Its object is to obtain information which will aid in the critical evaluation of prolonged human pregnancies. It is recognized that there is a gross difference in controlling the details of duration of pregnancy in the human being and in the lower animals. In the animal isolation is possible and coitus during heat makes a clearly defined beginning. In the human being, the last menstrual period may have little relation to the next ovulation and histories may be unreliable. The legal German maximum duration of pregnancy for the human being is set at 302 days post coitum.

The literature dealing with the horse, donkey, and cow is summarized. There apparently is no adequate veterinary observation to determine the development of the newborn animals in relation to variations in duration until gross postmaturity with fetal dystocia is reached. But it is interesting that the curves for variation in duration of pregnancy in the horse and in the woman are almost exactly the same. The variation in duration in the animals included in the study is of an order to support the concept that human pregnancy might continue for 302 days after coitus. In the horse the extremes are 280 and 370 days. The short duration probably means nothing but the upper extreme is almost 40 days beyond the average of 331 days. It should be noted, however, that the chance of pregnancy in the horse lasting beyond 365 days is only 0.2 per cent. The vast majority of pregnancies last between 320 and 345 days in the horse.

Similar variations are reported to occur in the other animals mentioned.

A consideration of the causes of variation in duration of pregnancy in these animals leaves little which can be directly carried over to the human being. It can be readily demonstrated in animals that there is a species variation. Pregnancy in the mare mated with the donkey is longer than that in the mare mated with the male horse. Variations of pregnancy duration in various species of horses and cows are listed. Species can be made to change the pregnancy duration by the addition of other species' genes to the strain. Average duration is less in multiple pregnancies but this obviously brings in other factors. The average duration is slightly longer ($1\frac{1}{2}$ to 3 days) when the fetus is a male. Poor general physical condition seems to prolong pregnancy. Seasonal variations occur and may be related to available nourishment and exercise. Age of the animal may be a factor.

No original material is presented but the report contains a useful summary of literature which is not readily available. An adequate bibliography is attached.

J. L. MCKELVEY.

Tscherne, E., and Engelhart, E.: *New Viewpoints on the Question of Prolonged Pregnancy*, München. med. Wchnschr. 87: 996, 1940.

In discussing the subject of prolonged pregnancy Tscherne and Engelhart feel that several points should be considered carefully, viz., (1) the length of the menstrual cycle, since the usual calculation of the delivery date is based on the twenty-eight-day cycle; (2) if the delivery date is ten days or more after the correctly determined date, the danger to the baby increases, especially in older primiparas. In a series of 1,222 cases the mortality figures varied from 7 to 19 per cent; (3) that the great danger to the baby should make us watch these patients carefully, not to wait too long before using operative measures and to consider induction of labor in time and, in the presence of complications, to consider cesarean section; (4) to verify the diagnosis of prolonged pregnancy through the objective information offered by determining with x-ray the proximal epiphyseal center of the tibia. If this diameter is near 7 mm., a prolonged pregnancy is very probable.

The authors also discuss the theory that the cause of the prolongation is a disturbed relationship between the placenta follicular hormone and the corpus luteum hormone, which theory seems to be strengthened by the fact that the hormone assay of the placenta in these cases shows subnormal values of follicle hormone.

C. E. PROSHEK.

Hosemann, H.: **The Law Concerning Duration of Pregnancy**, München. med. Wehnschr. 87: 715, 1940.

Hosemann studied the records and statistics of the largest obstetric clinics in various countries and concluded that the application of the old Rule of Naegele to determine the duration of pregnancy is still the most practical. The only change necessary to get better results is to modify this rule for those large groups of women in whom the cycle may be longer or shorter than twenty-eight days. In these cases the author suggests that the number of days that differ from the twenty-eight-day cycle be added to or subtracted as the case may be.

C. E. PROSHEK.

Cruickshank, Lewis G.: **Leucorrhea in Pregnancy; A Study of 200 Cases**, J. Obst. & Gynaec. Brit. Emp. 47: 109, 1940.

In this study the author has attempted to correlate the cause of leucorrhea by means of the relative proportion between epithelial cells and leucocytes, the character of the bacterial flora, the hydrogen-ion concentration of the vaginal contents, and the state of the vaginal epithelium in respect to glycogen deposition. The types were divided into Type I, a pure Döderlein flora; Type II, Döderlein bacilli mixed with a fair sprinkling of smaller gram-positive bacilli with perhaps one or two gram-negative bacilli; Type III, a mixed flora consisting of a great variety and number of organisms, chiefly small gram-positive and gram-negative cocco-bacilli. Spirochetes, comma bacilli, and leptothrix were searched for. The presence or absence of *Trichomonas vaginalis* or the hyphal filaments or blastospores of the parasite of vaginal thrush were specially looked for. In the cervical smear the relative proportion between mucus and epithelial cells and pus cells was noted and a diligent search for gonococci was made.

Two-hundred pregnant women supposed to be suffering from leucorrhea were examined. Twenty per cent showed a normal vaginal flora. Cervical lesions including erosions were found in nearly 40 per cent of the cases. In more than half of these, however, there were other causes of leucorrhea. Gonorrhea accounted for four cases among the two hundred. The parasite of vaginal thrush was found to be the cause of the leucorrhea in 25 per cent of the cases. The *Trichomonas vaginalis* parasite was found in 40 per cent of the cases and was found to be the most common offender. Eight cases were unclassified. In general, the recovery was associated with a change in the bacterial flora, and a return of the pH to between 4 and 5.

WILLIAM BERMAN.

Items

American Congress on Obstetrics and Gynecology

Special Notice

The committee which is sponsoring the next American Congress on Obstetrics and Gynecology, to be held in St. Louis on April 6 to 10, 1942, represents the only organization outside of governmental bodies which has attempted to unite the efforts of voluntary and other agencies to carry out the widely disseminated plans for the care of women and children and believes that in this time of stress, there should be a definite interest in the welfare of the mothers and babies of the nation. Opportunity for the presentation of advances in obstetric and gynecologic knowledge will be afforded to the many groups interested in these problems at a nationwide gathering of this kind. The Directors of the project believe that, notwithstanding the war situation, the Congress should be held at the stated time and are proceeding with their plans to make of this an outstanding gathering. Further details of the program will be communicated as these are made available. Inquiries may be addressed to the Central Office, 650 Rush Street, Chicago, Illinois.

Notes on the preliminary program will appear in the March issue of the JOURNAL.

Postgraduate Courses in Obstetrics at Chicago Lying-in Hospital

Five postgraduate courses in obstetrics, each of four weeks' duration, will be offered at the Chicago Lying-in Hospital between January 12 and June 6, 1942. These are sponsored by the Illinois State Department of Health and the Children's Bureau of the U. S. Department of Labor. The features of the program consist of observations on current managements of normal and abnormal states of the pregnant, parturient, and puerperal patient. Lectures, demonstrations, clinics, and other teaching means augment the operating room and birth room observations, and ward round discourses. The course is run on a non-profit basis. A deposit of \$25.00 is required on registration, \$10.00 of which is refunded at the completion of the course. All the members of the department participate in giving the courses. Additional information and application blanks may be obtained by request from Postgraduate Course, Department of Obstetrics and Gynecology, 5848 Drexel Avenue, Chicago, Illinois.

American Board of Obstetrics and Gynecology

The general oral and pathologic examinations (Part II) for all candidates (Groups A and B) will be conducted at Atlantic City, N. J., by the entire Board, from Wednesday, June 3, through Tuesday, June 9, 1942, prior to the opening of the annual meeting of the American Medical Association.

Application for admission to Group A, Part II, examinations must be on file in the Secretary's Office not later than March 1, 1942. It will greatly facilitate the work of the Board if applications are filed as far as possible in advance of the closing date for their receipt.

Formal notice of the time and place of these examinations will be sent each candidate several weeks in advance of the examination dates.

Candidates for *reevaluation* in Part II must make written application to the Secretary's Office before April 15, 1942.

As previously announced in the Board booklet, this fiscal year (1941-1942) of the Board marks the close of the two groups of classification of applicants for examination. Thereafter, the Board will have only one classification of candidates, and all will be required to take the Part I examinations.

The Board requests that all prospective candidates who plan to submit applications in the near future request and use the new application form which has this year been inaugurated by the Board. The Secretary will be glad to furnish these forms upon request, together with information regarding Board requirements. Address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pa.

Rules Governing the Award of "The Foundation Prize," American Association of Obstetricians, Gynecologists and Abdominal Surgeons

1. The award which shall be known as "The Foundation Prize" shall consist of \$150.00.

2. Eligible contestants shall include only (a) interns, residents, or graduate students in Obstetrics, Gynecology or Abdominal Surgery, and (b) physicians (with an M.D. degree) who are actively practicing or teaching Obstetrics, Gynecology or Abdominal Surgery.

3. Manuscripts must be presented under a nom de plume, which shall in no way indicate the author's identity, to the Secretary of the Association together with a sealed envelope bearing the nom de plume and containing a card showing the name and address of the contestant.

4. Manuscripts must be limited to 5,000 words, and must be typewritten in double-spacing on one side of the sheet. Ample margins should be provided. Illustrations should be limited to such as are required for a clear exposition of the thesis.

5. The successful thesis shall become the property of the Association, but this provision shall in no way interfere with publication of the communication in the Journal of the Author's choice. Unsuccessful contributions will be returned promptly to their authors.

6. Three copies of all manuscripts and illustrations entered in a given year must be in the hands of the Secretary before June 1.

7. The award will be made at the Annual Meetings of the Association, at which time the successful contestant must appear in person to present his contribution as a part of the regular scientific program, in conformity with the rules of the Association. The successful contestant must meet all expenses incident to this presentation.

8. The President of the Association shall annually appoint a Committee on Award, which, under its own regulations shall determine the successful contestant and shall inform the Secretary (James R. Bloss, 418 Eleventh Street, Huntington, W. Va.) of his name and address at least two weeks before the annual meeting.

Books Received

PREECLAMPTIC AND ECLAMPTIC TOXEMIA OF PREGNANCY. By Lewis Dexter, M.D., Research Fellow in Medicine, Harvard Medical School, and Soma Weiss, M.D., Hersey Professor of the Theory and Practice of Physic, Harvard University, etc. In collaboration with Florence W. Haynes, Herbert S. Sise and James V. Warren. 415 pages with 44 illustrations. Little, Brown and Co., Boston, 1941.

MOTHER AND BABY CARE IN PICTURES. By Louise Zabriskie, R.N., Director, Maternity Consultations Service, New York City, etc. Second edition, revised and reset. 208 pages with 204 illustrations. J. B. Lippincott Company, Philadelphia, 1941.

OBSERVACIONES SOBRE LA CLINICA DEL PUERPERIO. Por Carlos Alexander Ruelas. Universidad Nacional Autonoma de Mexico, Facultad de Medicina. Editorial Cultura, Mexico, D. F., 1941.

DISEASES OF WOMEN. By Harry Sturgeon Crossen, Professor Emeritus of Clinical Gynecology, Washington University School of Medicine, etc., and Robert James Crossen, Assistant Professor of Clinical Gynecology and Obstetrics, Washington University School of Medicine, etc. Ninth edition, entirely revised and reset. 948 pages with 1127 engravings, including 45 in color. The C. V. Mosby Company, St. Louis, 1941.

GYNECOLOGY AND FEMALE ENDOCRINOLOGY. By Emil Novak, Associate in Gynecology, the Johns Hopkins Medical School, etc. 605 pages with 425 illustrations, many in color. Little, Brown and Company, Boston, 1941.

THE BLOOD BANK AND THE TECHNIQUE AND THERAPEUTICS OF TRANSFUSIONS. By Robert A. Kilduffe, Director, Laboratories, Atlantic City Hospital, etc., and Michael DeBakey, Assistant Professor of Surgery, School of Medicine, Tulane University of Louisiana, etc. 558 pages with 214 illustrations and one color plate. The C. V. Mosby Company, St. Louis, 1942.

SEMIOLOGIA DO OVARIO, com um estudo particular da citologia vaginal. Par Dr. Francisco Victor Rodrigues, Professor de Clinica Ginecologica da Faculdade Fluminense de Medicina da Universidade do Brasil, etc. Casa do Livro Limitada, Rio de Janeiro, 1941.

I'M GONNA BE A FATHER. By Bob Dunn. Illustrated. David McKay Company, Philadelphia, 1941.

OUR SEX LIFE. A Guide and Counsellor for Everyone. By Fritz Kahn. Second, revised edition. 459 pages. Illustrated. Alfred A. Knopf, New York, 1942.

HERNIA. By Alfred H. Jason, Consulting Surgeon, Long Beach Hospital, etc. 1325 pages with 355 illustrations. P. Blakiston Company, Philadelphia, 1941.